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Arterial Hypertension
Bronchiogenic Cancer
Modern Medicine
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The Pathogenesis of Arterial Hypertension

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When the results of research by clinicians, biochemists, physiologists, pathologists and nutritionists are assembled, analyzed and integrated, it appears that the pathogenesis of "primary" or "essential" and malignant hypertension has been determined in spite of the fact that all pressor substances and mechanisms have not been positively identified.

Epidemiology

High blood pressure has rarely been found in the Negroes living in the wilds of Africa, but its incidence in all parts of the United States and in some Central American countries and West Indian Islands is reported to be higher in Negroes than in the better nourished whites and natives of those regions. Bantu laborers in South Africa have developed hypertension following recovery from beriberi or pellagra. It also developed in many who had been on deficient diets while prisoners of the Germans or Japanese for many months, after liberation had made available their usual diets. Other such prisoners did not develop high blood pressures, possibly because their diets had not lacked the same essentials or because during convalescence, were more adequate. After the siege of Leningrad was raised, hypertension and hypertensive cardiovascular-renal disease developed epidemic proportions.

These epidemiological findings are substantiated by recent studies on the effects of drastic food restriction on young normal adults and on some with high blood pressures. These investigations showed that a very low caloric diet reduced both normal and high blood pressures; that caloric restriction may be as effective as sodium restriction in reducing high blood pressure. During recovery from semistarvation, cardiovascular dynamic balance often becomes so disturbed that heart failure develops in subjects with normal hearts. Others, whose blood pressures had been normal prior to the period of drastic food restriction, developed hypertension; and those whose pressures had previously been elevated developed higher pressures after the restrictions were removed.

It has long been known that people who are overweight are more apt to have hypertension than are those whose weight is normal or below normal. It is not generally appreciated that the high calorie diets of the overweight are frequently insufficient for the proper utilization of the large quantities of carbohydrate, protein and fat consumed plus the metabolic requirements of the individual; that the obese frequently show signs of nutritional deficiency. It is also not known that many adults, regularly employed at high wages, and many children in private and public schools, have been found to select diets deficient in more than one essential nutriment. Surveys, made in various parts of the United States and Canada, have shown that some forty per cent of the diets have been deficient in riboflavin and ascorbic acid. About forty-four per cent of the workers in a Southern California airplane factory were found to have a deficient intake and low blood levels of ascorbic acid.

There is an increasing amount of evidence that the incidence of hypertension is higher among those whose nutrition is inadequate because of ignorance, poverty or the improper selection of food by those who could afford to be well nourished. This suggests that familial habits of eating may be more important than heredity in explaining the prevalence of high blood

pressure in certain families. Some of these nutritional deficiencies may be due to methods used in producing, preserving, processing and cooking the foods. These methods reduce their content of essential nutriments to make a diet, that should be adequate, more or less deficient.

Disease, prolonged hard mental or physical work, undue fatigue, excitement, emotion, exposure to extremes of temperature or to rapid changes in weather or altitudes may so increase the metabolic requirements that a normal intake of certain essential nutriments becomes inadequate. Certain therapeutic agents, especially when their administration is not properly controlled, certain chemicals used in industry, some normal metabolites in high concentration, or abnormal metabolites in normal concentration may limit the absorption, assimilation or action of essential metabolites and respiratory enzymes, causing nutritional failure identical with that produced by relative or absolute nutritional deficiency. The incidence and multiplicity of causes of nutritional failure make it a factor which may be of especial importance in the pathogenesis of the hypertensive syndromes.

Biochemistry and Physiology

Factors which increase metabolic requirements, mentioned in the last paragraph, cause neurogenic stimulation of the pituitary and hypersecretion of its adrenal corticotropic hormone to increase adrenal cortical metabolism. The injection of highly purified pituitary adrenocorticotropic hormones has been found to cause a rapid fall in the ascorbic acid and cholesterol levels in the adrenal cortex of rats and guinea pigs, but does not cause ascorbic acid depletion in other tissues. The utilization of ascorbic acid is reported to accurately reflect the activity of the adrenal cortex. It is known that its administration increases the ability of an individual to withstand extreme cold, heat, infection and the toxic effects of certain therapeutic agents. These findings plus the fact that its concentration is higher in the adrenal than in other tissues, make it evident that ascorbic acid is essential for normal adrenal cortical function. Sodium, tyrosine, thiamine, pantothenic acid and other vitamin B factors are also required for its proper functioning. Cortical hyperfunction increases the demands for these essentials, and the amounts available must be more than "adequate" if the production of abnormal cortical hormones is to be prevented.

As ascorbic acid seems to be necessary for normal protein metabolism, it is essential for normal kidney and liver function. The concentration of riboflavin is higher in the kidney than in other tissues. It seems to be as essential to renal cortical metabolism as ascorbic acid is to adrenal. It is required for the deamination of amino acids by oxidation in the renal cortex. Rats on diets adequate except in their riboflavin content or on diets adequate except for a very high tyrosine content, develop hypertension. The injection of phenylalanine, from which tyrosine may be synthesized in vivo, has been shown to raise the blood pressure of animals with experimental and humans with clinical hypertension. When riboflavin is lacking, deamination of amino acids by decarboxylation with the production of pressor amines and renin increases in slices of renal tissue in vitro. Pressor amines, one of the most potent of which is tyramine, cause local arteriolar constriction and further limit cellular nutrition to increase the synthesis of pressor amines and initiate changes resulting in the activation of the renin-hypertensin pressor mechanisms.

The nutritional requirements of the liver, pituitary gland, adrenal medulla and other chromaffin tissues participating in the regulation of blood pressure levels are high for all essential nutriments but are not as specific as those of the kidneys and adrenal cortex. Almost any relative or absolute deficiency may therefore modify their activities in the regulation of blood pressure levels.

Hypersecretion of the adrenocorticotropic hormone by the pituitary gland is decreased when protein intake is limited. The reduction of blood pressure levels of normotensives and hypertensives on semistarvation diets is probably due to the depressing ef-

fect of their low protein content on pituitary function. As tyrosine is a component of the thyrotropic and adrenotropic hormones of the pituitary, their secretion must be decreased when insufficient amounts of this essential amino acid are available. As it is a constituent of epinephrin, renin and hypertensin which when deaminized by decarboxylation is transformed into the potent pressor amine, tyramine, tyrosine seems to play an important part in both normal and abnormal pressor mechanisms.

It is evident that if the nutritional supply is to be optimal for normal tissue function under all ordinary conditions, it must contain more than "adequate" amounts of the essential nutriments required by the usual metabolic demands in addition to the amounts required for the metabolism of the protein, carbohydrate and fat needed to maintain nitrogenous equilibrium and to cause weight to approach closely the "ideal" for height. If the occupation or temperament of an individual are such that there are frequent or prolonged demands for hyperfunction of certain glands; or if there is exposure to chemicals which inhibit the formation or action of respiratory enzymes, even an optimal diet becomes insufficient.

Adrenal cortical hyperfunction causes the blood levels of cortical hormones to rise. This high concentration of normal corticoids causes arteriolar constriction because it inhibits renal deamination by oxidation and so stimulates the formation of pressor amines, which process activates the renin-hypertensin humoral pressor mechanism; or because, by its effects on the pressor center in the medulla or on the depressor nerve endings in the left ventricle, aorta and carotid sinus, it causes a neurogenic type of arteriolar constriction and activates the pressor mechanism found in chronic experimental or clinical hypertension. Abnormal corticoids, which are formed when prolonged or frequently repeated cortical hyperfunction causes nutritional failure, inhibit the renal amino acid oxidases and cause arteriolar contraction. Other sterones, for example the sex hormones, may when increased in amount, have similar effects.

The pressor amines formed when deamination of amino acids by oxidation is inhibited and, by decarboxylation, increased, cause local arteriolar constriction in the renal cortex. This causes renal ischemia and reduces pressures and flow in the vessels of the renal cortex, to further limit its nutrition. Thus a vicious circuit is set up which seems to activate the renin-hypertensin humoral pressor mechanism.

Adrenal cortical hyperfunction may, when it has caused nutritional failure and the formation of abnormal corticoids, so modify the rate of formation or composition of the catechol precursors of epinephrin that there is hypersecretion of the medullary hormone or the production of an abnormal pressor substance which is more potent or longer acting than the normal hormone. The abnormal corticoids or medullary hormone may be isomers of the normal metabolites. The arteriolar constriction caused by the medullary hyperfunction may initiate the vicious circuit leading to the activation of the hypertensive mechanisms. Inhibition of the hepatic or renal destruction of normal or abnormal corticoids and medullary metabolites will result in higher blood levels and so have the same effects that hypersecretion has on the pressor mechanisms.

Experimental Hypertension

High blood pressure has been produced in animals by the production of increased intracranial pressure and by trauma to the nervous connections of the pituitary or to the brain stem, both of which cause hypersecretion of the adrenocorticotropic hormone. Destruction of the depressor nerve endings in the left ventricle, aorta and carotid sinus results in a neurogenic type of hypertension which differs in some ways from the clinical and from the experimental hypertension produced by other methods.

Chronic experimental hypertension can regularly be produced by methods which induce sufficient renal ischemia. Most investigators have applied Goldblatt clamps to one or both renal arteries to produce the ischemia, but some have preferred to encase

the kidneys in an inelastic plastic or silk capsule, and others to ligate the poles of one or both kidneys. The renal ischemia inhibits the amino acid oxidases; increases deamination by decarboxylation with the formation of pressor amines; and activates the renin-hypertensin humoral pressor mechanism. Increased amounts of renin and hypertensinase have been found in the blood of animals during the initial stages of experimental hypertension and in patients with acute nephritis but not in chronic experimental or clinical hypertension. This makes it appear that some other pressor mechanism, probably neurogenic in origin, replaces the humoral mechanism when the hypertension becomes chronic. As chronic hypertension does not develop when renal ischemia is produced in animals that have been adrenalectomized or hypophysectomized and as adrenalectomy causes a lowering of the blood pressure in animals with experimental hypertension, these glands seem to be involved in its pathogenesis.

The renin-hypertensin humoral pressor mechanism stimulates the hypersecretion of the adrenal corticotropic hormone by the pituitary. If such pituitary hyperfunction is sufficiently prolonged or frequently repeated, the resulting nutritional failure causes the production of abnormal pituitary hormones which at all blood levels have tropic effects on the adrenal cortex. When adrenal cortical hyperactivity causes the supply of its essential nutriments to become deficient, abnormal corticoids are formed which activate the neurogenic pressure mechanism, causing chronic hypertension.

Selye believes that when there is sufficient interference with renal blood flow to cause the blood pressure in the renal cortex to approach the osmotic pressure in its cells, the kidney is transformed into an endocrine gland which secretes a pressor substance, probably renin, in an effort to restore normal blood pressure in the cortical vessels. He seems to have overlooked the effects of ischemia on cellular nutrition.

Trueta and his coworkers have shown that stimulation of the sympathetic nerves of the kidney or the injection of toxic chemicals into the blood stream can cause such severe spasm of the afferent arterioles that cortical blood flow is arrested and all renal arterial blood shunted through the juxtamedullary glomeruli and vasa recti. Constriction of the afferent arterioles and cortical necrosis have been demonstrated in the kidney on the side on which there had been crushing injuries to a lower extremity. These investigators suggest that hypertension may develop because of the increased pressure required to force all renal arterial blood through the reduced vascular bed created by this "shunt." It seems more probable that hypertension develops when the neurogenic or humoral constriction of the afferent arterioles causes some renal cortical ischemia but not the elimination of all cortical blood flow with necrosis of its parenchyma.

There is evidence that altered function of the neurohypophysis may cause hypersensitivity to normal and abnormal adrenal corticoids and epinephrin and so may contribute to the activation of abnormal pressor mechanisms. An hereditary sensitivity to these metabolites may be responsible for the high familial incidence of hypertension reported by many clinicians.

Pathology

The diffuse or adenomatous hyperplasia of the adrenal and pituitary glands found in association with essential or malignant hypertension resembles the thyroid hyperplasia due to a deficient intake of iodine. It seems probable that the adrenal and pituitary hyperplasia is also a reaction to a specific type of nutritional failure. Pantothenic acid deficiency has been reported to cause such changes in the adrenal gland.

Congenital or acquired pathology causing rernal ischemia has been found in association with a type of chronic hypertension very similar to chronic experimental hypertension. Urinary tract disease causing increased pressures within, and dilatation of, the renal tubules creates intratubular urinary pressures approaching the cortical blood pressures and the osmotic pressures of the renal parenchyma. The blood supply and nutrition of the cells are thus reduced and the production of pressor amines increased to activate the renin-hypertensin humoral

pressor mechanism. The toxic products of infection in the kidney, lower urinary tract or other part of the body may inhibit the formation or action of renal amino acid oxidases, thus serving to activate this pressor mechanism. Abnormal metabolites produced because of infectious or metabolic diseases may cause the type of nutritional failure in the pituitary or adrenal glands, kidneys or liver that activates abnormal pressor mechanisms.

The tendency of the abnormal pressor mechanisms to gradually increase nutritional failure and the formation of pressor metabolites can account for the insidious onset and slow but steady progress of "primary" or "essential" hypertension. When this process is speeded up because abnormal pituitary adrenal corticotropic hormones increase the production of abnormal adrenal corticoids or inhibit their destruction in the liver and kidneys "malignant hypertension" develops.

As nutritional failure causes: first, tissue depletion; second, biochemical change; third, functional change; and fourth, anatomical change, it explains the pathological changes as well as the clinical course of "essential" and "malignant" hypertension.

Therapy

Various methods now being used in the treatment of hypertensive states support this hypothesis as they either depress pituitary and adrenal function or general metabolism or increase adrenal and renal blood flow to improve the nutrition of these tissues. Low protein intake decreases pituitary function and general metabolism. Low sodium intake depresses adrenal cortical activity. The thiocyanates are general metabolic depressants but have no specific effects on the production of the abnormal pressor substances. Splanchnisectomy inhibits neurogenic arteriolar constriction in the adrenal glands and kidneys and thus improves their nutrition. Low protein, low salt diets, relatively high in vitamins, such as the "rice diet," and the various types of splanchnic resection advocated by neurosurgeons should therefore lower blood pressure levels.

To be most effective, therapy should be directed at restorating normal function when changes are still reversible and at limiting the production of pressor substances when irreversible changes have already developed. A low protein, low salt diet containing more than adequate amounts of riboflavin, ascorbic acid and vitamin B complex and enough tyrosine for the normal function of the pituitary and adrenal glands should be most effective in restoring normal pituitary, adrenal, renal and hepatic function. When there is already much irreversible change causing neurogenic arteriolar constriction, the effectiveness of such therapy is increased by the administration of substances like veratrine which have a prolonged depressor effect. The author has found this type of therapy to be of great value in the management of "essential" hypertension. The protein content of the diet should be just sufficient to maintain nitrogenous equilibrium; its caloric value such that the weight "ideal" for height is approached.

"Experimental hypertension" due to renal ischemia will not be greatly benefitted by such therapy because of the irreversible changes presented by the Goldblatt clamps, inelastic capsules, or ligatures used in its production. This type of treatment might, however, slightly reduce blood pressure levels and slow the progress of the hypertensive processes. It has been found to lower both systolic and diastolic blood pressure levels, to prevent the development of azotemia and to delay the rate of progress of the disease in patients with long-standing severe hypertension and considerable irreversible change.

Conclusions

"Primary" or "essential" hypertension develops when minimal and slowly increasing nutritional failure due to nutritional deficiency, to the inactivation of respiratory enzymes and essential nutriments, to their depletion as a result of hyperfunction, or to the diminished blood flow caused by neurogenic or humoral arteriolar constriction, activates the renin-hypertensin pressor mechanism and an abnormal neurogenic pressor mechanism associated with adrenal

cortical dysfunction. When the nutritional failure develops more rapidly and causes continued secretion by the pituitary of a metabolite which stimulates adrenal cortical activity and the liberation of abnormal corticoids concerned with the neurogenic pressor mechanism, or when it so affects the liver and kidneys that the destruction of corticoids is greatly reduced, the syndrome of "malignant" hypertension develops.

This hypothesis, which, now, can be expressed only in most general terms, is supported by the epidemiology of hypertension, by the pathological, biochemical, physiological and anatomical changes characteristic of the hypertensive syndromes, by their clinical course, by the results obtained with various types of therapy; and by the methods used in the production of "experimental hypertension."

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—Concluded on page 563

SPECIAL ARTICLE

Angina Pectoris

This summarization attempts to cover all of the known therapeutic information on the subject and is designed as a time-saving refresher for the busy practitioner.

Reprints available*

Angina pectoris is a syndrome marked by paroxysmal pain which is substernal or immediately to the left of the sternum. It is accompanied by suffocation and syncope and occurs in attacks which are precipitated by effort, excitement, heavy meals, exposure to cold, or while at rest or sleeping. Although there are various causes of angina pectoris the one which causes it most commonly is an anoxia or undernourishment of the myocardium. The available coronary blood flow is insufficient to meet the temporarily greater demands upon the heart for work. It is considered to be a symptom of a serious underlying cardiac disturbance rather than a specific disease. It is also known as angina of effort, breast pang, sternalgia, sternodynia and *orthopnoea cardiaca*.[1-4]

Incidence

The anginal syndrome was believed to occur more frequently in the so-called "white-collar" class rather than in the working class of people but this has been shown to be false. However, a study of the poverty-stricken malnourished peasants of Puerto Rico has shown that they rarely develop angina pectoris.[5] This, despite the fact that they are severely anemic. Some have shown that even a mild anemia may be a secondary cause of angina[6] whereas others have stated that even a severe anemia has not caused it and that the anemia must be associated with a form of coronary atherosclerosis.[7] Angina pectoris may develop during the third or fourth decade of life but it is more common in the fifth, sixth and seventh decades with the highest incidence in the sixth decade. It occurs more commonly in men than in women, the ratio being approximately 4.3 to 1.[8] Jewish people are said to develop it quite commonly whereas Negroes rarely do.[2] In a study[8] of a series of patients it was reported that death occurred most frequently in the first year when it had been established that the condition was coronary arterial disease accompanied by angina pectoris. More women having the condition survived than men. It was also discovered that the survival rate was longer when the condition developed later in life than when it developed between the years of 30 and 39. A study of the survival curve over a period of years revealed that the mortality rate was constant at approximately 10 per cent of those surviving each year after the first. The mortality rate was increased if one of the following conditions also prevailed: congestive heart failure, cardiac hypertrophy, hypertension, previous myocardial infarction and significant electrocardiographic abnormalities.

Etiology

As stated, angina pectoris is caused by anoxia of the heart muscle but there also may be involved a mechanical and chemical irritation of the nerves which supply the heart. Coronary sclerosis resulting in a coronary insufficiency is most commonly the cause of angina pectoris but other conditions also are capable of causing this anoxia of the myocardium. Included in this group are: (a) Aortic insufficiency, bringing about a low diastolic blood pressure which decreases the coronary blood flow

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even though an hypertrophied left ventricle increases its demand for oxygen; (b) a decrease in coronary blood flow as a result of a syphilitic aortitis causing a narrowing or blocking of the entances of the coronary arteries; (c) an infectious condition such as rheumatic fever which invades the wall of a coronary artery; (d) rheumatic or syphilitic disease of the aortic valve with free aortic regurgitation; or (e) high grade aortic stenosis or mitral stenosis accompanied by distortion of the coronary orifices. These are all organic factors. Functional factors involved include: general anoxemia; marked anemia; very rapid heart rate of the type where short diastole causes insufficient circulation in the coronary arteries like that occurring in paroxysmal tachycardia.[2, 9] A recent investigation has correlated the clinical manifestations of coronary heart disease with the pathologic findings in the heart. In those cases of angina pectoris, which were studied, evidence, not only of coronary arteriosclerosis was found, but also there was present in one and usually two of the three major coronary arteries an area of old complete occlusion. Thus any increased demand on the heart for work would naturally lead to myocardial anoxia. No infarcts were found in some cases because it was believed that a collateral circulation had developed because the occlusion took place so slowly. In other patients there was evidence of an old myocardial infarct.[10]

Any etiologic agent, which places a sudden additional strain upon the heart bringing about an increase in that organ's rate or blood pressure, will lead to an attack of angina. Thus an angina attack may be brought on by excitement, mental strain, physical effort, a heavy meal, a systemic infection, exposure to cold, anemia or hyperthyroidism. Vasomotor changes in the coronary circulation may be brought on by food in the stomach and exposure to cold and as shown by the fact that smoking may induce a typical attack in some patients. Many may experience an attack while eating, resting or sleeping. If the coronary arteries are normal, anemia and hyperthyroidism probably will not cause angina pectoris. In those cases of angina caused by anemia or hyperthyroidism correction of the causative conditions usually results in disappearance of the attacks unless the patient exerts himself to an unusual degree.

Symptoms

The attacks of angina pectoris usually follow a typical pattern. There is developed gradually a feeling of heaviness in the chest, usually in the middle or upper third of the substernal region, finally developing into a severe, viselike, crushing pain forcing the patient to cease all activity. The pain may be confined to the area described or it may radiate into the left shoulder and down the left arm to the elbow and sometimes along the ulnar aspect of the forearm to the wrist and even the tips of the fingers. It may radiate to the neck, one or both jaws, teeth, upper abdomen, right shoulder, arm and forearm or to the mid-dorsal or left scapular region. A sense of fright and of impending death often accompanies the pain. Because the attack is usually brought on by exertion in some form, immediate rest will bring relief within 2 to 3 minutes in most cases, thus shortening the length of the attack. If the attack continues for longer than 15 minutes coronary occlusion should be suspected. Belching to remove gas may appear to relieve the attack but rest is the chief remedy. The patient may have difficulty in describing the aching, burning or cramp-like pain and may refer to it as a sensation of heaviness, tightness, choking or constriction. The more severe attacks often cause immobility of the patient in a certain posture and during the entire attack he may not groan despite the pain.

Cases of angina pectoris have been reported in which the pain begins in a region other than the substernal area. These areas are the ones to which the pain radiates when it follows the typical course.[11] In many of the cases it finally localizes in the chest. If the pain begins in one of the other areas and does not radiate to the chest some condition other than angina may be responsible.

Some few cases of angina pectoris are accompanied by dyspnea, palpitation and abnormal sweating, lightheadedness and syncope. In some instances an attack may

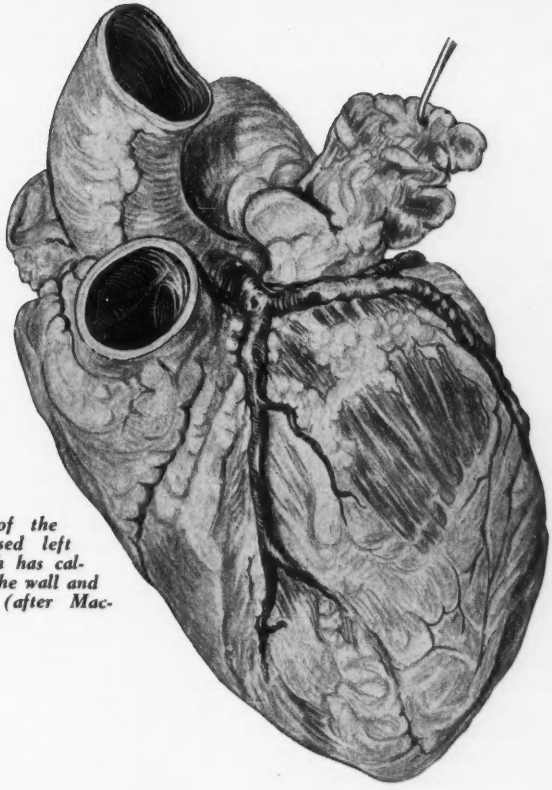

Fig. 1. Left side of the heart showing exposed left coronary artery which has calcification patches on the wall and nodular thickenings (after Mackenzie).

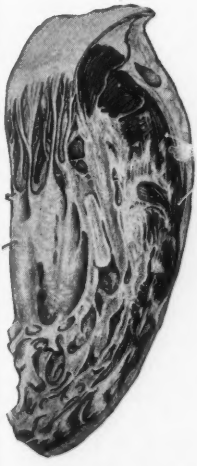

Fig. 2. Heart wall showing chronic fibrotic myocarditis.

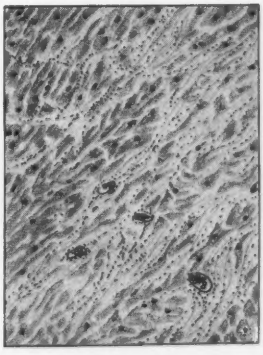

Fig. 3. Microscopic drawing showing myocardial fibrosis.

occur while the patient is at rest or asleep but this is most common in cases of advanced coronary artery disease. It is believed to be due to the greater reduction in coronary blood flow at this time than in cardiac work.[2, 9]

An attack of angina pectoris is usually followed by a sensation of soreness in the chest and certain skin areas are hypersensitive. This may persist for some time after the attack. After the chest pain subsides there may be a numbness persisting in one of the points of radiation. There may be flatulence, particularly if the pain radiates to the epigastrium.[2]

Mild attacks of angina pectoris usually do not incapacitate the patient unless he is the highly emotional type of individual. If the patient is rather stolid and not upset over the possibility of such attacks he may have to be dealt with firmly in respect to the reduction of his activities to a degree sufficient to abort any future attacks.

The clinical course of angina pectoris may follow a rather typical pattern in some individuals but more frequently it varies considerably. Some few patients will have a mild attack with no recurrence for the next several months or years whereas others may have severe attacks at frequent intervals and die suddenly within a very short period of time because of the development of ventricular fibrillation or cardiac arrest during an attack. Most individuals have seizures over several months or years varying considerably, dependent upon the general health of the patient, temperature of the environment, as well as changes in the coronary arteries and their relationship to the collateral circulation and its effectiveness. If collateral circulation, to those areas in which myocardial anoxemia occurs, is developed sufficiently there may be no recurrence for a long time and in some there may be permanent relief of the condition. Development of myocardial infarction involving the area which had a relative anoxia previously will result in the replacement by insensitive fibrous tissue of that portion of the heart muscle from which came the abnormal stimuli and as a result there will be no recurrences of angina attacks.

Physical Signs

No uniform objective signs are observed in angina pectoris because the syndrome is a physiologic phenomenon induced by various causes. No characteristic physical changes occur during or between the seizures other than those related to the underlying cause. The heart rhythm is generally regular and the organ itself may be enlarged although not necessarily so. A rise in arterial pressure may be noted during an attack because approximately 50 per cent of the patients also have hypertension. There may or may not be pallor during the seizure. If the patient is going through an attack angina may be indicated by the rigidity of the body during the height of the pain and the relief, so noticeable as the pain diminishes. In some patients angina is indicated by an anxious, perspiring, agonized appearance; the facies is a worried, pale type; and instead of rigidity there is a constant struggling for some position of relief.

If coronary sclerosis is the underlying cause for the angina the electrocardiogram is of value in diagnosis as changes in the tracings indicate. However, the presence of coronary sclerosis or insufficiency is not precluded if the tracing happens to be normal. Patients may show normal tracings between attacks and abnormal ones during the attack. If the tracings are abnormal between seizures they are accentuated or additional changes occur during the attack. Common changes are exhibited in the T wave which may be inverted or diminished in amplitude and in the S T segment which may be depressed in one or more leads. There also occur commonly varying degrees of auriculoventricular or intraventricular block and in some cases may be observed the tracing exhibited by myocardial infarction, either anterior or posterior.

Diagnosis

A test known as the anoxemia test has been devised as an aid in diagnosis. An electrocardiogram is made of the changes brought on by induced anoxemia. An

electrocardiogram is made first and then the patient at rest in bed is given a mixture of 10 per cent oxygen and 90 per cent nitrogen to breathe for 20 minutes or less if he becomes uncomfortable. After this forced anoxemia another electrocardiogram is made and usually changes in the tracing are noted if the patient has the angina syndrome. The test is considered to show positive results when the arithmetical sum of the R S—T deviations in leads I, II, III and IV F is greater by 3 mm. or more than that of the control or when the T wave in lead I is completely reversed in direction and the R S—T deviation in that lead is 1 mm. or more. A positive response may also be indicated by a complete reversal of the direction of the T wave in lead IV F. Some patients may experience some degree of anginal pain during the test which is considered to be good evidence also of the presence of the syndrome even if there are no changes in the tracings.[12,13] A study of a number of cases has shown that positive results were obtained in 53 per cent of 92 patients with angina pectoris whereas 82 patients with very slight signs of coronary disease showed negative results with the exception of 1 patient.[14]

Exercise tests are also used and involve the taking of an electrocardiogram before and after exercise. The exercise usually consists of walking over a two-step staircase at a certain rate of speed. When pain or dyspnea develops the tracing is taken.[15] In a study of patients subjected to this test positive electrocardiographic changes were observed in 50 to 60 per cent of patients having angina pectoris. The results were considered positive when there was more than 1.3 mm. depression in the limb leads of the R S—T segment and more than 2 mm. in lead IV R; when the tracing showed characteristics of that noted in acute myocardial infarction or bundle branch block; or change in the sign of the T wave unless this occurred only in lead III.[16] This test is more simple and safe than the anoxemia test.

A positive result in either of these tests is considered as corroborative evidence that the diagnosis is correct but a negative result either in the tracing or non-production

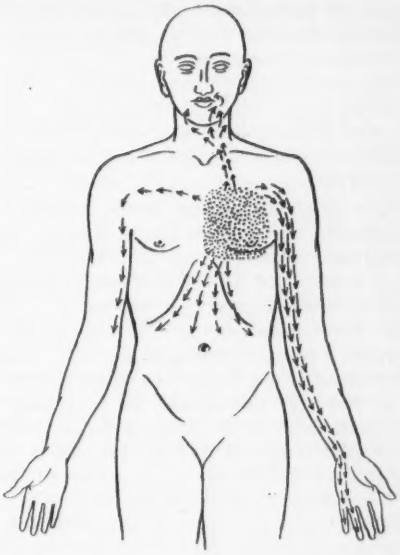

Fig. 4. Dotted area shows section of the chest where the pain usually originates. Arrows indicate pathways of radiating pain.

of pain does not preclude the possibility of coronary heart disease.

In addition to the tests described above it is necessary to evaluate carefully the case history, data from laboratory tests, any physical signs revealed by examination, and characteristics of the attacks. In some cases which do not follow the typical pattern diagnosis is made more difficult by the anxiety of the patient. The pain must be studied in respect to whether it is caused by a cardiac or extracardiac factor; its location, character, radiation and duration; and the ways by which relief is provided.

Differential Diagnosis

In properly diagnosing angina pectoris it is necessary to eliminate the possibility that the symptoms may result from another condition. There are many conditions which cause pain closely resembling that occurring in angina. These include esophageal hiatus

hernia, cardiospasm or spasm of the esophagus, osteoarthritis of the upper dorsal spine, gallbladder disease, scalenus anticus syndrome, arthritis of the left shoulder joint, intercostal neuritis, pleuritis, pericarditis, severe flatulence, tumor of the lung or mediastinum, neurocirculatory asthenia (soldier's heart, effort syndrome) and anxiety neurosis.

The pain which occurs in the first three conditions named may be located in the substernal region but can be differentiated by investigation of factors which bring about its development, how long it lasts and the methods by which relief is obtained. The pain from one of these three conditions is not induced by physical exertion but may be brought on as a result of excitement or of eating a large meal. The pain is not relieved by rest as it is in angina and it lasts much longer than in the latter condition. In esophageal hiatus hernia the pain is frequently brought on as the patient reclines or if he bends forward sharply to tie his shoes. Some state that a pain may be present in the right shoulder[2] whereas others state that it occurs at the top of the left shoulder because of irritation of the left dome of the diaphragm.[9] In this condition atropine usually affords relief and nitroglycerin may or may not be successful. Diagnosis of this condition can be confirmed by x-ray examination after ingestion of a barium meal. The patient is placed on a tilt table with his head down so that the barium meal can flow into the hernia.

In osteoarthritis of the dorsal spine there may be pain in the substernal region and anterior chest. In this condition minor movements such as raising the shoulder, use of the arms or bending, twisting or turning over in bed may bring on the pain. The pain may not be brought on by walking if the shoulders are maintained in a fixed position. No relief occurs when nitroglycerin is administered. X-ray diagnosis is very useful in determining this condition.

In neurocirculatory asthenia and states of anxiety, fatigue or nervous tension, the pain is a sticking or aching precordial pain rather than substernal and is located in the region of the cardiac apex. In some patients this pain may radiate down the left arm to the fingers and up toward the left shoulder but not to the substernal region. There generally are pains elsewhere in the body. The pain may be sharp or sticking and of very short duration but there will persist for several hours a dull, aching sensation. Exercise or excitement may precede the pain but it does not occur during such periods as in angina. There usually is no structural heart disease present.[9] In neurocirculatory asthenia there will be observed also certain symptoms of vasomotor instability such as a flushed face, low blood pressure and periods of breaking out into profuse perspiration.[2] There may be observed also extreme fatigue and certain personality changes.

Substernal discomfort also may be brought on in sensitive or apprehensive patients as a result of cardiac arrythmias. Such a condition can be differentiated from angina pectoris by its characteristic transiency, its association with subjective awareness of cardiac irregularity and the frequency of repetition without regard to any excitement or physical activity.[9]

Prognosis

The prognosis varies considerably with each patient and with the underlying cause and is always uncertain. The subsequent course in angina brought on by an organic disease depends upon the type and extent of structural damage. The prognosis is poor in those cases where only a little excitement or exertion induces a severe and prolonged attack and very poor if the attack occurs while the individual is at rest. Although patients who have mild attacks sporadically as a result of some unusual activity can expect to live many more years their hopes should not be raised too high. They must be instructed to avoid any such precipitating factors. However, it is still possible for death to result from one attack. Death may occur as a result of some heart condition but in older patients also may be caused by neoplastic diseases, pneumonia, renal failure associated with hypertension or in cerebral vascular accidents. If the condition has a

functional basis the patient has a chance of living the normal life span.

Recent studies of 497 cases followed for at least 12 years have shown the average duration of life in 445 to be 7.9 years but in the 52 remaining it was 18.4 years so that the average figure for the entire group was almost 10 years which is far more optimistic than previous figures available.[17] Another study of 3440 cases showed that the mortality rate in the first year after diagnosis was 18 per cent and 10 per cent each year thereafter.[8]

Complications

Acute myocardial infarction and congestive heart failure frequently occur in angina pectoris sufferers. The former usually develops at some time in about 50 per cent, and the latter in about 25 per cent. After the acute myocardial infarction is eliminated the seizures of angina usually begin again if the individual returns to his earlier activities. In some cases the patient may have no angina seizures for long periods of time. Very occasionally the patient may find permanent relief.

Congestive heart failure as a complication of angina pectoris is considerably more serious and results in death for most patients in less than 2 years. The rest which is necesary to treat this condition usually alleviates the attacks of angina. The general spread of the myocardial anoxia is also a factor. Only a limited myocardial reserve can be built up even with severe restriction of activity and a long rest period.

Therapy

Many drugs are employed in the treatment of angina pectoris with varying results. However, it is important that the patient be instructed to avoid any activity which might induce an attack. He soon learns what activities are responsible. Everything he does must be done slowly. He must learn to allow ample time for everything so that he does not hurry his dressing or his meals and so that he does not hurry to catch a street car, bus or train whether he be going to work or traveling. Climbing of stairs should be avoided but when necessary they should be climbed very slowly. Excitement or emotional stimulation, straining and heavy lifting should be avoided whenever possible.[9] It has been suggested that the regimen necessary for the greatest prolongation of life includes none of the things usually required of the average individual in a highly competitive world.[3] Although it is believed that altitudes of 10,000 to 12,000 feet are not harmful, airplane travel should be avoided if the attacks occur following slight exertion or at rest. Some physicians ask that coitus be avoided as well, although some believe that in certain individuals such a restriction might precipitate an attack.[3] The person should not be made to live the life of a total invalid for this usually causes anxiety but he should learn to distribute his physical activities over longer periods of time. Some patients may prefer more frequent attacks rather than to restrict their activities to such a degree.

Diet

The patient should be instructed to avoid full heavy meals and particularly gas-forming foods or foods which do not agree with the individual. The three meals each day should be equal in size and relatively light. In order to avoid overeating at any one meal it may be more suitable to have 4 or 5 smaller meals in a day's time. Coffee may induce cardiac pain in some patients. In certain cases hydrochloric acid with the meals or carminatives after meals may be helpful.

In various surveys conducted of patients with angina pectoris overweight has been found to be a disadvantage.[18,19] A reducing diet should be prescribed so that the heart will have less work to perform during any physical activity. Thyroid extract is not indicated for reducing purposes in patients with coronary disease. Because an attack of angina is more apt to be induced with less exertion than normally after the individual has eaten the patient should be advised to rest for 30 to 45 minutes after every meal. It is not necessary to lie down for rest in a chair is adequate.

There is some controversy over the use of alcohol and tobacco. Some state that

smoking should be avoided because of its effect in increasing the heart rate and the blood pressure and in decreasing the peripheral blood flow and possibly its direct effect upon the flow of blood through the coronary arteries. Others have found that a comparison of individuals with and without angina pectoris showed that tobacco did not appear to play an important part in the cause of the condition but its use did aggravate or precipitate attacks in some instances.[20] In another study it was shown that smoking appears to be a contributory factor, particularly in the younger person.[21]

Alcohol in the form of whisky or brandy and taken with very little water has been found to provide relief of symptoms and improve the condition of the patient. This is especially of value in some cases in which the nitrites are ineffective. However, not too much alcohol should be taken because of its action in abolishing fatigue which in turn leads the patient to overexertion.[2,3,21] Other workers have shown that alcohol did not shorten the duration of the attack to any extent and did not increase the individual's capacity to work. In addition some patients were made worse and others, although showing no real improvement, felt better. This increased sense of well-being is believed to be due to the sedative effect in reducing anxiety and apprehension and could be just as effectively achieved with sedatives.[22]

Temperature

Cold is also a factor which influences the ease of induction of an attack. Therefore an angina pectoris patient should be advised to wear warm clothing and gloves during cool weather. The patient should avoid walking through snow or against the wind if possible because walking under such conditions increases the load on the heart. It is preferable for the patient to spend the winter season in a warmer climate if his financial status permits this.

Rest

Immediate rest and cessation of all physical activity or emotional excitement are important in relieving an angina attack. If the patient prefers, and many do, he need not lie down during the attack but may sit in a chair. If the attacks become more frequent and severe, rest in bed for a week to 10 days may be necessary.

Drugs

The drugs used in angina pectoris are divided into two types. The first type includes those which are used to relieve the seizure and the second type includes those which are given to prevent or reduce the occurrence of the seizure. Some drugs belong to both types. Their action is similar in that they dilate the coronary arteries and newly developed collateral vesels so that the coronary blood flow is increased. Those given to relieve the pain during an attack act faster and more effectively but their effect is less prolonged than that of the drugs used to prevent attacks.

Nitrites

Amyl nitrite and nitroglycerin are two of the drugs used to relieve seizures of angina pectoris. Although amyl nitrite has a more rapid action, nitroglycerin is preferred by most. Amyl nitrite is very convenient to carry in the form of the "pearls." A pearl is crushed in the handkerchief and the drug inhaled. Relief from the pain occurs in 30 seconds to 1 minute. Amyl nitrite is available in capillary tubes encased in a specially woven cocoon which keeps the glass from cutting the fingers. Unfortunately this drug has an objectionable odor and may cause more side reactions than nitroglycerin.[3,23]

Nitroglycerin is given in as small a dose as will be effective so as to reduce the possibility of side reactions which include a drop in blood pressure, palpitation, throbbing headache or flushing of the face and, in some, severe discomfort for 48 hours. Some find that a ⅓ mg. (1/200 gr.) dose is usually sufficient whereas others recommend twice that quantity.[3,23] The drug is given preferably in the form of hypodermic tablets which are more quickly soluble. The tablet should be held under the tongue. With this drug the full effect does not take place for 2 or 3 minutes. Because of the possibility of side reactions some recommend a dosage of 0.15

to 0.3 mg. (1/400 to 1/200 gr.) in new patients until the amount of reaction is determined.[24] Some recommend the smaller dose routinely.[25] Others have directed the patient to remove the remains of the tablet as soon as relief has occurred, although many patients have taken large doses without any difficulty. All patients with angina pectoris should be advised to carry tablets of nitroglycerin with them at all times and if rest does not relieve the attack in one minute they should be instructed to use a tablet. It may be necessary to reassure the patient that the use of amyl nitrite or nitroglycerin is not habit forming and that frequent use is not harmful. It should be explained that the drug does not deaden pain as a narcotic does but relieves the pain by bringing about an improved circulation of blood to the heart. However, the patient also should be cautioned against neglect in avoiding attacks just because the drug is available. If two tablets fail to relieve the attack the patient should be advised to contact the physician because myocardial infarction may have developed.

Nitroglycerin and amyl nitrite are also used to prevent attacks of angina. Many patients with angina are occupied at tasks which frequently bring on a seizure or it may be precipitated by eating a meal. In many of these cases the seizure can be prevented by taking the drug just prior to performing the task. In cases where the attack comes following a meal the drug should be taken either before or immediately after the meal. In some patients 12 to 20 tablets may be necesary each day. It is believed that such use is not harmful but here again the patient should not fail to avoid the precipitating factors whenever possible.[9,25]

There are other related compounds used in the therapy of angina pectoris which are longer-acting, namely erythrityl tetranitrate, mannitol hexanitrate and sodium nitrite. However, the disagreeable effects described previously are more frequent with these drugs. They have been found of value in lessening the number and severity of seizures in patients having many attacks within the 24 hour period and of particular value in those having attacks in the night. Erythrityl tetranitrate and mannitol hexanitrate are administered in doses of 15 to 60 mg. (¼ to 1 gr.) and are available in 15 to 30 mg. (¼ to ½ gr.) tablets. Sodium nitrite is not quite so expensive as the aforementionel drugs but in some cases it may be extremely irritating to the stomach. Some have found it more effective when given with sodium or potassium iodide. Sodium nitrite is administered in tablet or capsule form in doses of 60 mg. to 0.2 Gm. (1 to 3 gr.).[3] The dose must be carefully regulated for the patient since the average dose is 60 mg.

Sedatives

Mild sedatives are of value in the therapy of angina pectoris, particularly in those patients who are anxious about their condition or easily upset emotionally. They reduce their mental activities, assure a restful sleep and to a certain extent reduce the severity and number of the attacks. The longer acting barbiturates such as phenobarbital are indicated. The dose usually given is 15 to 30 mg. (¼ to ½ gr.) 3 times daily.[9] Sedatives are particularly helpful in aiding the patient to approach mealtime in a relaxed manner.[26] Chloral hydrate may be used if preferred. Codeine sulfate has been found of use in patients who are elderly, thin and have arteriosclerosis but who are still leading active lives despite the enlarged heart and anginal attacks. It is given in doses of 8 mg. (⅛ gr.) 4 times a day for 10 days.[27, 28] Opiates should not be given for the relief or prevention of a seizure because of the danger of addiction when employed repeatedly. In cases where the pain is so severe that no other drug will relieve it morphine may be necessary.

Papaverine hydrochloride has been reported by some to have value in doses of 0.1 Gm. (1½ gr.) 4 times a day in the therapy of angina pectoris.[29, 30] Others have found that even in doses of 30, 100 and 200 mg. (½, 1½ and 3 gr.) it did not increase exercise ability and effects were disappointing.[9, 31] However, one of the original investigators later stated that he

believed it is of value in prophylaxis because it is a powerful coronary dilator. He believed that in this respect it could be as effective as quinidine and in addition it is not a depressant to the heart.[32,33] In experimental animals papaverine has been shown to bring about a definite increase in coronary blood flow but the duration of the effect is only 2 to 3 minutes.[33] The sedative action may be of use in some patients. The N.N.R. single dose is 30 to 80 mg.; the daily dose is up to 50 mg.; and the single dose which is said to be nontoxic is 1.0 Gm. (15 gr.)[34]

Xanthine Vasodilators

The xanthine vasodilators are believed by some to have value in the therapy of angina pectoris. This is a highly controversial subject for others have been unable to attain satisfactory results. In many cases the side reactions preclude their use. Such reactions include nausea and in some instances vomiting, a burning pain in the epigastrium or under the sternum, palpitation, dizziness, headache, nervousness and other minor complaints. The drugs usually used include theobromine and sodium acetate, theobromine and calcium salicylate and aminophylline. In some few cases a tolerance and a cross tolerance to these drugs have developed. For this reason some recommend that the drug be taken for 4 consecutive days weekly and omitted for 3 days and theobromine alternated with one of the theophylline products. A study of the effectiveness of the various drugs has shown that approximately equal effects (decrease in R S—T deviation) are obtained with 0.2 Gm. of aminophylline 3 times daily, 0.36 Gm. of theophylline with sodium acetate 4 times daily, and 0.45 Gm. of theobromine with sodium acetate 4 times daily. It was found that the time of appearance of the pain was not greatly affected by these drugs in patients with induced

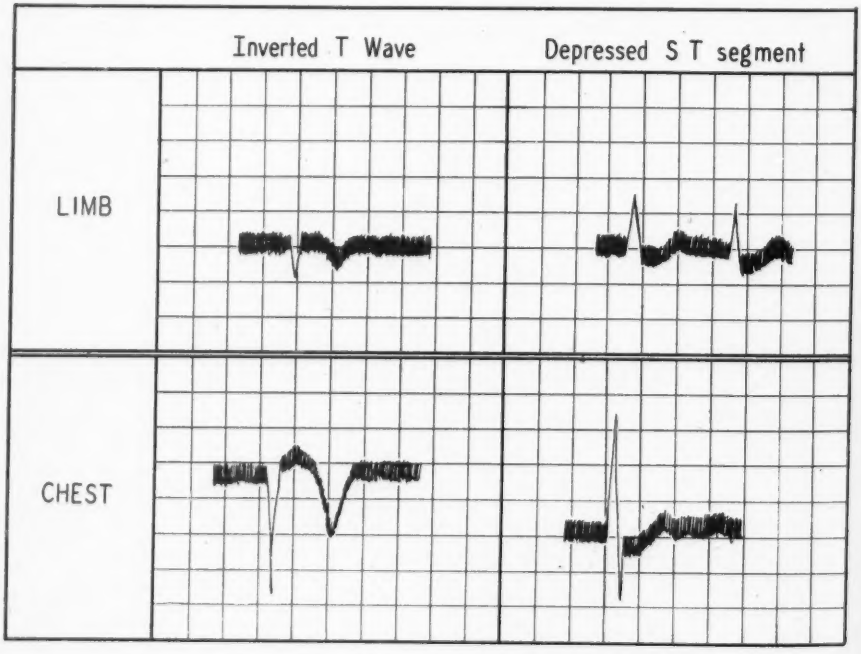

Fig. 5. Common changes in the electrocardiogram when coronary sclerosis is the underlying cause of angina pectoris.

anoxemia although previous studies had shown that a 26 per cent prolongation in the appearance time of the pain resulted when aminophylline in the same dose was taken 4 times daily.[35] Favorable changes were noted in the electrocardiogram and the onset of pain was delayed by intravenous administration of aminophylline[36] and theophylline with sodium acetate.[2] Further reports of the use of aminophylline showed 75 per cent of 68 patients were benefited while only 20 per cent received relief with placebos and sedatives.[37] Others reported that the patients noted no differences between the effect of the drugs and the placebos[38,39] and still others reported them as far from satisfactory.[40] However, some workers continue to recommend them.[41] Use of the drugs in many cases has been shown to produce a better therapeutic response in those patients having less severe and less frequent attacks than in those having a more advanced stage of coronary insufficiency.[2]. Theobromine and sodium acetate appears to be the preferred drug of some.[9,28] It is given orally in enteric-coated tablets in doses of 0.5 Gm. (7½ gr.) 4 times daily. Although other factors also have been responsible for improvement in the patient, withdrawal of the drug for several weeks usually resulted in a greater number of attacks. It is recommended that the xanthines at least be tried on the patient and if benefited should be continued and vice versa. Other investigators prefer theobromine and calcium salicylate in doses of 0.5 Gm. 3 times daily because it is least likely to cause side effects but on the other hand it is probably not so effective as the others.[23]

Digitalis

The position of digitalis in the therapy of angina pectoris does not seem to be well-established unless congestive heart failure or auricular fibrillation develops. In patients where there is a shortness of breath following exertion to a degree less than that necessary to precipitate an attack digitalis may be indicated. The physician must often decide, based on the progress of the patient, whether digitalis is of value or whether its use should be discontinued.

Nicotinic Acid

Although oral administration of moderate doses of nicotinic acid were found to cause little if any improvement in angina pectoris cases[42] subjective and objective evidence of improvement maintained for 6 months has been reported following intravenous infusion of 100 to 300 mg. of the drug (6 infusions in 3 weeks).[43] Orally too large a dosage was necessary to make any changes in the electrocardiogram. Such large oral doses resulted in an excessive degree of peripheral flushing which is not desirable.

Iodides

Some patients (12 per cent) who did not respond to other measures were found to show improvement when given 1.0 Gm. (15 gr.) doses of potassium iodide in enteric-coated tablets 3 or 4 times a day.[28]

Cobra Venom

Exercise tolerance has been shown to be increased following use of cobra venom in patients who did not respond to other drugs. The cobra venom was administered in doses of 10 mouse units (1 cc.) 3 times daily for the first day. This was followed by one daily injection for 7 days and then bi-weekly as a maintenance dose. The only untoward effect was local pain from the injection but this was not severe enough to warrant discontinuance of the drug. The action of cobra venom was not that of a coronary vasodilator because its administration did not hinder the changes in the electrocardiogram after exertion.[44,45]

Khellin

Some time ago an extract of the seeds of the *Ammi visnaga* plant, which grows wild along the eastern shores of the Mediterranean, was found to give relief in angina pectoris. It was administered in a single dose of 100 mg. (1½ gr.) intramuscularly and repeated if necessary. If oral administration was desired 50 to 100 mg. were given 3 times a day. Further investigation of this drug, Khellin, is being conducted.[46]

Testosterone Propionate

The use of testosterone propionate in therapy of angina pectoris is another highly controversial subject. Its use was first reported in 1939.[47] Favorable reports have shown that 91 per cent of 100 patients showed improvement for 2 to 34 months following injection of 25 mg. of testosterone propionate for 5 to 20 injections (11 average). The drug was given once or twice a week.[48,49] Another investigator also reported improvement in 7 out of 10 patients. It was noted in these cases that more response was shown by patients with stable electrocardiograms than by those showing progressive deterioration.[50] On the other hand, another report of its use in angina pectoris stated that it could not be concluded that the drug was of any value because angina pectoris varies so in its clinical course.[51] A further report led to the conclusion that neither intramuscular injection of testosterone propionate nor oral administration of methyl testosterone shows any value in angina pectoris. However, testosterone has shown some value in relieving the discomfort of the chest at the time of the male climacteric or the similar precordial ache of neurocirculatory asthenia in patients of the same age group as those with angina. Another worker has reported also that 8 patients at the period of the male climacteric responded to testosterone and not to vasodilator drugs.[53] Testosterone appears to have a vasodilator effect and does improve the sense of well being of the patient. Some are of the opinion, however, that it will never occupy an important role in this type of therapy.[9]

Ethyl Chloride, Procaine

Because referred visceral pain is relieved by infiltration of procaine into the tender areas in the somatic reference zone investigation has shown that complete and prolonged relief of pain can be accomplished in angina pectoris and acute myocardial infarction by ethyl chloride spray or procaine infiltration of the somatic trigger areas along the sternal borders.[54]

Surgical Procedures

If the patient is in a serious stage of angina pectoris in that even the smallest amount of exertion induces a seizure or it occurs while he is resting or asleep and he does not respond to prolonged rest or medical treatment surgical intervention may be necessary. Years ago complete removal of the thyroid gland was carried out but this practically has been abandoned because of the great risk and the resultant serious complications. As a substitute for this thiouracil has been tried for its possible value. Some benefit has been observed but there is still the danger of toxic effects from the drug. It is hoped that propylthiouracil will overcome this problem to some extent.[3,55–58]

Frequently used is the paravertebral sympathetic block by means of alcohol injected into the upper 4 or 5 thoracic sympathetic ganglia or the corresponding rami communicantes. It is extremely important that this procedure be done by an experienced person and that the injection be placed accurately. Some have recommended insertion of the needles followed by an x-ray checkup before the alcohol is injected.[59] This procedure is relatively safe for complete failure has been reported in only 10 per cent of the cases. Good results have been reported.[60] Some state that approximately 50 per cent of the patients have marked relief and in some the relief is permanent. Although there is relief of the anginal syndrome any activity on the part of the patient which might cause coronary artery insufficiency will result in a feeling of pressure beneath the sternum.[2] The use of this method may be followed by sensory disturbances in the chest and upper extremities, and painful intercostal neuritis for several months.[28] Pleurisy, pneumothorax and toxic myelitis are also possible complications.[9]

If the alcohol injections fail altogether or provide only temporary relief it may be necessary to remove the upper 4 or 5 thoracic ganglia. This is particularly indicated when the pain of the seizures is distributed unilaterally. This procedure is more risky than alcohol injection but it is not so

great a risk as laminectomy with bilateral rhizotomy which is indicated when the pain is entirely substernal or when it radiates both right and left.[2,9] Some have stated that this procedure carries very little greater risk than the sympathectomy and in addition it is a bilateral operation which can be finished in one stage.[61]

Other surgical procedures have been used but they are generally highly specialized, used chiefly by the inventor and still in the experimental stage.

Associated Conditions

It is important in treating angina pectoris that co-existing diseases be treated as well. These may include thyrotoxicosis, anemia, active peptic ulcer, spastic colitis and others. Proper treatment of anemia or thyrotoxicosis if either is present will improve the patient's resistance to attacks and may even result in permanent relief. If extrasystoles are present their elimination may bring about relief from seizures. Biliary colic, caused by gallstones, should be treated by surgery (if the patient can stand surgery), which usually results in decreasing the frequency of attacks. If the patient has diabetes the dosage of insulin should be carefully regulated because a low blood sugar level is not tolerated by patients with angina pectoris. The safer procedure is to maintain a slightly higher level than is desired. Too low a blood sugar level causes a rise in the pulse pressure, minute volume output of the heart and the ventricular rate. Thus the work of the heart is increased and may induce an angina seizure.[62] Constipation should be avoided because straining at stool may induce an attack.[9]

Angina Decubitus

Angina decubitus is not only difficult to treat but the prognosis in such a condition is grave. The xanthine derivatives given orally rarely reduce the incidence of seizures during the night. Sedatives given at bedtime may help. Some relief has been attained by the use of aminophylline given intravenously in doses of 0.46 Gm. (7½ gr.) in the evening. Restriction of the diet in respect to its sodium chloride content and administration of a mercurial diuretic to bring about dehydration may help in some cases.[61] Bed rest for a week to 10 days is indicated in order to prevent the development of acute myocardial infarction which frequently follows. Nitroglycerin has little or no effect in this type of attack. Relief from the pain may occur promptly if the position is changed to that of sitting or standing.

Psychotherapy

Psychotherapy of angina pectoris is often of considerable importance. It is necessary for the physician to allay the fears which the patient may have such as fear of death. The patient should be given encouragement concerning the prognosis so that he does not worry nor indulge in emotional episodes. A great deal can be done to lessen the frequency and severity of the attacks by helping the patient to have a normal mental attitude in regard to his condition. There is probably no anxiety which is more overwhelming than that which accompanies an attack of angina pectoris. With each attack the anxiety increases and as the attacks increase the anxiety appears to be justified, finally resulting in a vicious circle which is difficult to interrupt. The simplest psychotherapeutic measures will relieve the situation. It is important in every case that the physician not adopt a fatalistic attitude toward the patient for if he shows discouragement it is impossible to expect the patient to do otherwise.

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National Gastroenterological Association 1949 Award Contest

The National Gastroenterological Association again takes pleasure in announcing its Annual Cash Prize Award Contest for 1949. One hundred dollars and a Certificate of Merit will be given for the best unpublished contribution on Gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy.

All entries for the 1949 prize should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies accompanied by an entry letter, and must be received not later than April 1, 1949. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

Northwestern University Presidency

Dr. James Roscoe Miller, dean of Northwestern's Medical School, has been elected president of Northwestern University and will assume office on July 1, 1949.

Dr. Miller will become the twelfth president of the University, succeeding Franklyn B. Snyder, president since 1939, who will retire September 1, 1949 at the age of sixty-five in accordance with the University's retirement policy.

Duke-Sponsored Medical Course Is Announced for Next Spring

The North Carolina Medical Postgraduate Course, sponsored by the Duke University School of Medicine, will be held March 21-24.

Early Diagnosis of Bronchiogenic Carcinoma

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Glen Cove, New York

I. Introduction

Carcinoma of the lung, until recently, was considered a relatively rare disease, and thus less stress was placed upon it in the literature. Postmortem and clinical studies now show that in recent decades bronchiogenic carcinoma has increased in frequency to a point where it now ranks fairly high among malignant growths, accounting for approximately ten per cent of cancer deaths. It is estimated that ten to fifteen thousand persons die annually from the disease in the United States. Likewise, less stress has been placed upon carcinoma of the lung because of the feeling of hopelessness and a fatalistic attitude taken toward its treatment on the part of the profession at large. This attitude must change, for with the surgical contribution of total excision of the lung, with resection of the mediastinal lymphatic structures, there will result a fairly high five year survival rate, *provided* definitive treatment is instituted early. The emphasis of cancer educational programs directed toward the public has been successful in alerting the patients to the danger signs of cancer, but I believe now that this emphasis should be directed to the doctors. The index of suspicion on the part of the doctors must be raised so that the early signs and symptoms of carcinoma of the lung will be recognized, thus enabling definitive treatment to be instituted and thereby the present interval, averaging nine months, between the onset of symptoms and the institution of treatment, will be materially lowered. The encouraging feature of this disease is that 98 per cent of patients with carcinoma of the lung have symptoms referable to the chest. With "red flags" available, it is the duty of each doctor to recognize them, and utilize the available diagnostic armamentarium, cooperating thereby with an alerted public who seek out medical advice. Too often, the thoracic surgeon is confronted with the stock reply that no chest x-ray was recommended, since the doctor did not think the cough was serious.

II. Incidence

There has been an absolute, as well as a relative, increase in carcinoma of the lung, according to autopsy statistics, and this is ascribed to the aging population, improved methods of diagnosis, and greater accuracy in histologic differentiation. Fifty years ago, 17 per cent of the population in the United States was above 45; in 1940 the percentage had risen to 26.5 per cent, and it is estimated that by 1990 it will be 40 per cent (1). The increasing incidence of bronchiogenic carcinoma is thus to be expected, since it occurs almost exclusively in older age groups, i.e., in the fifth and sixth decades, with the average at 52.5 years. Furthermore, the widespread use of x-rays, particularly the periodic mass survey methods, the increasing appreciation of the value of the bronchoscope, and the heightened cancer consciousness of the profession, have served to bring to light many cases of cancer which in former years masqueraded as tuberculosis, unresolved pneumonia, bronchiectasis, lung abscess and more recently atypical pneumonia. It now appears to be one of the most frequently encountered malignant neoplasms, being preceded in the male only by the stomach as a primary site.

It is an interesting, though unexplained fact, that carcinoma of the lung is pre-

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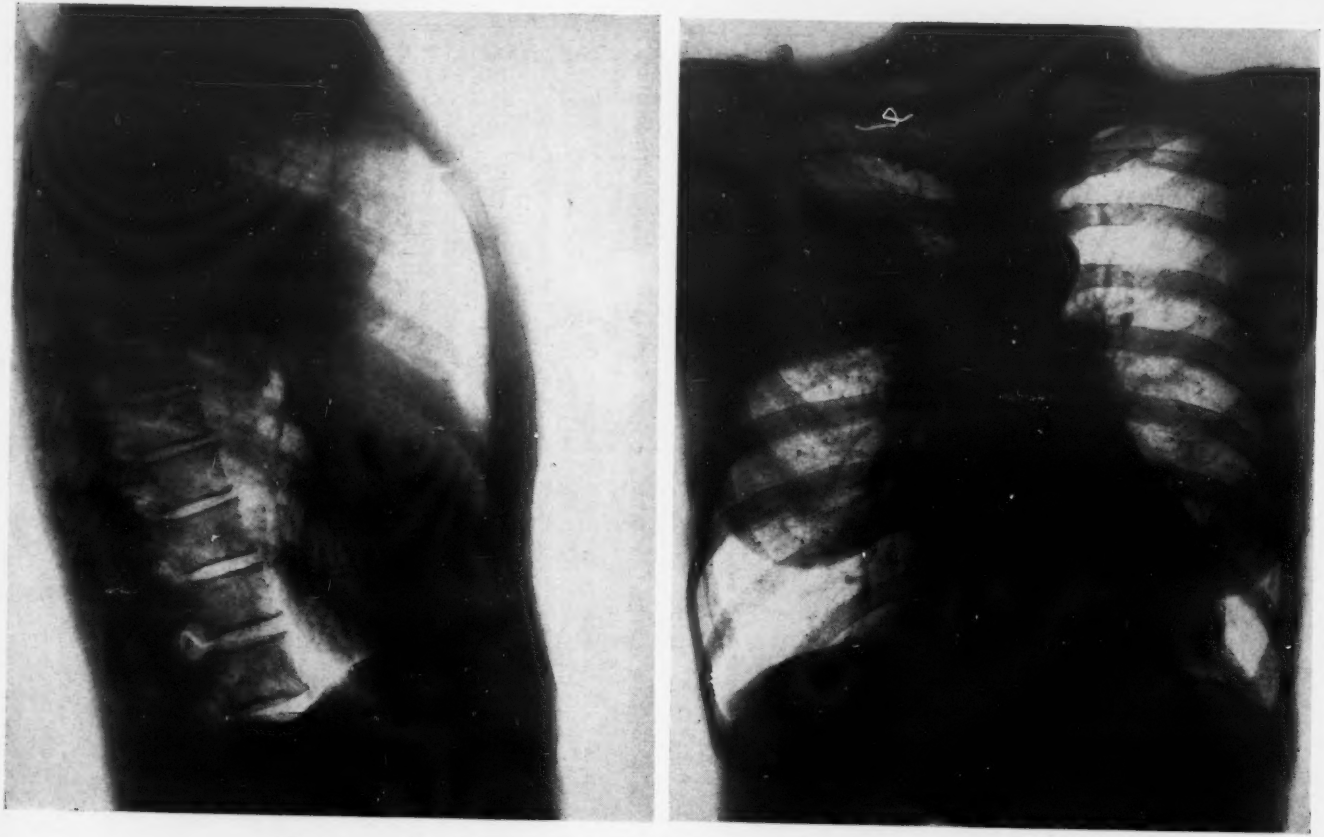


Figs. 1 and 2. These films demonstrate a peripheral tumor which was entirely asymptomatic and was discovered on routine chest survey. At operation, it proved to be a squamous cell carcinoma which was resectable.

dominantly a disease of the male sex, with the average ratio being eight to one. As for racial predominance, it is less common in Negroes, with a ratio reported by Oschsner and DeBakey of two to one in favor of the white race (2).

III. Etiology

Like cancer elsewhere in the body, there is no proved carcinogenic agent known, though tobacco smoking, particularly cigarette smoking, inhalation of gasoline and tar derivatives, inhalation of noxious gases and fumes incident to various occupations have been indicted in many reviews of this subject, but there is no experimental proof that any of these is a factor in the pathogenesis. Except for the Schneeberg miners inhaling radioactive cobalt dust, pneumoconiosis has not increased the incidence of carcinoma of the lung among miners. Although there is little direct evidence to support the belief that chronic irritation may be a cause of lung carcinoma, it is a known fact that the disease occurs chiefly in heavy smoking men of the laboring class, who work in dusty atmospheres, and whose lungs sustain considerable wear and tear (1). Therefore, one is justified in the belief that exposure to chronic irritation, whether it be chemical or infectious, in a susceptible individual, over a period of years, may be suspected of a carcinogenic effect on the bronchial mucosa.

IV. Pathology

Seventy-five per cent of bronchiogenic carcinomas arise in a major bronchus, and thereby the bronchoscopist is aided in establishing a biopsy diagnosis. The tumor arises in the majority of cases from the undifferentiated cells lining the basement layer of the bronchial mucosa, which gives rise to three types of tumors, i.e., (1) Epidermoid or squamous cell type; (2) Adenocarcinoma and (3) Anaplastic type, or so-called "oat-cell" or spindle type cell. The epidermoid variety occurs more commonly in males, is slower growing, metastasizes later and metastasizes less frequently. In females, the adenocarcinoma is more common, occurring frequently in the periphery of the lung; it is more malignant, and has a higher incidence of intracranial metastases. Pathologists have correlated the degree of malignancy of bronchiogenic carcinoma with the cellularity of the tumor, on the theory that the more cellular the structure, the more malignant; and also the greater radiosensitivity. This fact is borne out clinically, for the slower growing epidermoid tumors respond best to surgery, and poorest to irradiation; whereas the oat-cell tumors give poor surgical results, but respond better to x-ray than other lung neoplasms. The tumor arising from the bronchial mucosa penetrates the bronchus and spreads by direct extension as well as by the lymphatics and blood channels. The lymphatic spread is centrally toward the hilar nodes and peripherally to the pleura, resulting in hemorrhagic effiusions. In 3047 collected cases of carcinoma of the lung reported by Ochsner and DeBakey (2), the incidence of metastases was as follows:

Regional nodes	72.5 per cent
Liver	33.3 per cent
Pleura	29.8 per cent
Bone	21.3 per cent
Adrenals	20.3 per cent
Kidney	17.5 per cent
Brain	16.5 per cent
Heart and pericardium	12.7 per cent

In those cases showing node involvement, 70 per cent were mediastinal, 18 per cent cervical, 7 per cent axillary, and 4 per cent supraclavicular.

Apical carcinoma presents some unusual features which distinguish it from tumors elsewhere in the chest. Its origin is from an apical bronchus, or sometimes in a lower cervical branchiogenic rest, and with its regional invasiveness infiltrates the brachial plexus, cervical sympathetic nerves, upper vertebrae and ribs, and soft structures, giving rise to the so-called Pancoast syndrome, i.e., Horner's sign, atrophy of the arm muscles and pain from brachial nerve involvement. Its location, rather than its cell type, differentiates it into this special category.

operation, it proved to be a squamous cell carcinoma which was resectable.

V. Symptoms

Carcinoma of the lung like cancer elsewhere in the body is notorious for its insidious onset and paucity of symptoms in the early stages. However, the encouraging feature of the disease, as pointed out previously, is that 98 per cent of the cases will have symptoms referable to the chest. The common picture is a man over forty with a persistent cough of a few months' duration, expectorating some blood-streaked sputum, an unexplained thoracic discomfort, and who may, or may not, have lost some weight. The key to early diagnosis is the consideration of its possible presence.

The initial symptom in about 85 per cent of the cases is a dry cough due to the irritation of the sensitive bronchial mucosa; the cough in time is productive of a watery or mucoid sputum, later becoming blood-streaked. As the tumor ulcerates hemoptyses occur, though massive bleeding is not common. Narrowing of the bronchus leads to a wheeze, and eventually, with complete blockage, there is atelectasis and recurring pneumonitis, due to the stasis. Not infrequently, there is a history of previous respiratory infection, a "grippe"-like condition, with a persistence of symptoms rather than a prompt and complete recovery.

It is important that not infrequently only one or two of these manifestations are present and occasionally the patient has no symptoms, the diagnosis being made from a routine x-ray of the chest. Cough is particularly difficult to evaluate, for the patient blames smoking as a rule. Any change in the cough must be distinguished, and especially to ascertain if there are any associated chest symptoms of recent development.

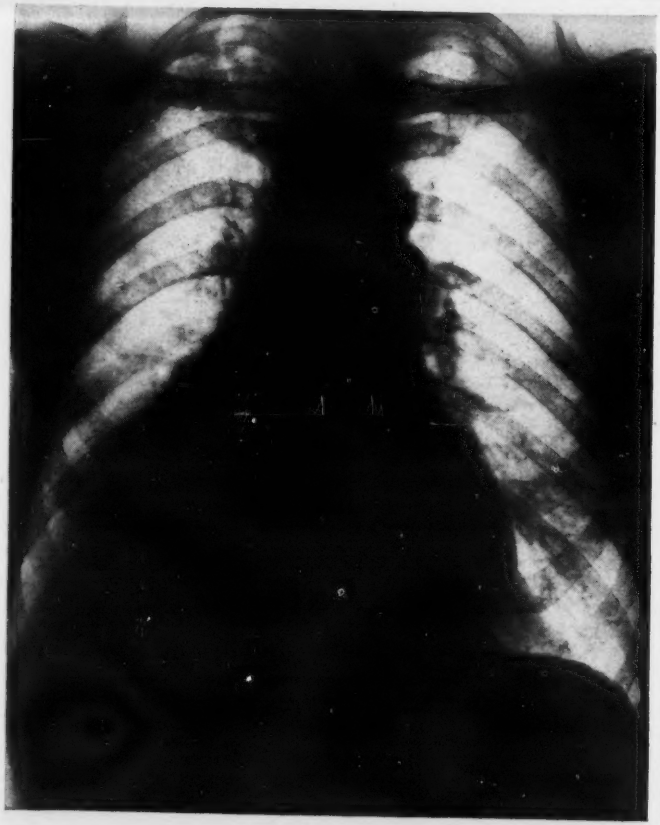
The development of hoarseness, Horner's sign, purulent sputum and clubbing of fingers and toes are manifestations of late stages of the disease, and frequently are signs of inoperability. We are more concerned with the early symptoms, for the key to cure is early diagnosis.

VI. Diagnosis

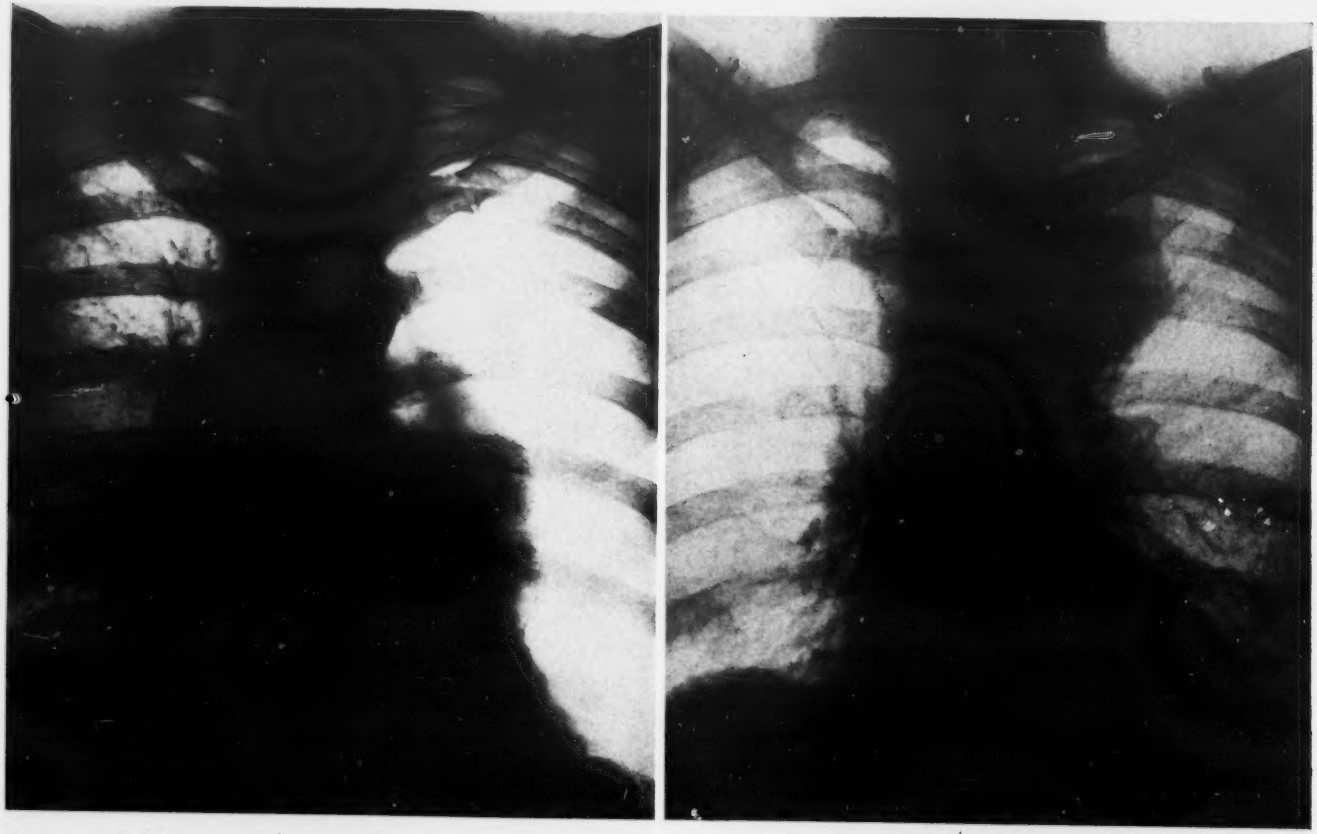
In the early stages, the physical signs of carcinoma of the lung are few or absent, but as the tumor progresses, there result atelectasis, suppuration, intrathoracic displacements, pleural involvement and eventually compression phenomena, all of which aid in the presumptive diagnosis of the disease. More often than not, the physical signs are of little help in diagnosis and frequently are appreciated only in retrospect.

The important diagnostic methods include the various types of x-ray examination (i.e., routine roentgenograms, kymograms, tomograms, and bronchograms), bronchoscopic examinations of the tracheobronchial tree, and finally cytologic examinations of the bronchial secretions and sputum. These are the chief aids in confirming the diagnosis in early lesions. For late lesions, we have available thoracentesis with examination of the pleural fluid for tumor cells (a step more helpful in prognosis rather than in treatment), thoracoscopic biopsy of pleural implants, and aspiration biopsy of node involvement or lung neoplasms in inoperable cases. The lung aspiration is not recommended as a routine procedure, and should be condemned for an early lesion. It is to be remembered that the resulting atelectasis due to bronchial obstruction may give a roentgen opacity out of proportion to the actual size of the tumor, and does not represent invasion of the lung. This point is important when surgery is considered, for the size of the opacity does not necessarily determine operability. One of the earliest signs of bronchial encroachment is localized areas of hyperillumination of the lung, indicating obstructive emphysema. This is best shown by taking films in inspiration and expiration, a simple and very helpful method which is frequently neglected. Centrally located lesions are often difficult to find roentgenologically without the aid of the kymograph, though serial roentgenograms will show their progress. Sometimes a small peripheral lesion will produce large mediastinal shadows representing involved nodes.

The greatest aid in diagnosis is the bronchoscope, for with this instrument we can obtain direct visualization of the tu-



Figs. 3 and 4. These films demonstrate atelectasis of the right lower lobe resulting from a small tumor located in the lower lobe bronchus. The shadow represents collapsed lung and not the extent of the tumor.



Figs. 5 and 6. The first film shows a total collapse of the left lung resulting from a spontaneous pneumothorax, which at first was presumed to be from a ruptured emphysematous bleb, but subsequent films (Fig. 6) over the next 6 months revealed the development of a tumor in the left upper lobe. At operation, this proved to be a squamous cell carcinoma. It is postulated that in the early stages of the tumor it partially obstructed a segmental bronchus, causing an emphysema in an area of the lung that ruptured under the stress of coughing. Spontaneous pneumothorax is a rare presenting sign of lung neoplasm, though obliterative emphysema is not.

mor, as well as section a piece of the tumor for microscopic examination in about 65 to 70 per cent of the cases. When the tumor is in the upper lobe, then with the aid of a special mirror the lesion can be seen, although biopsy is not possible. With upper lobe tumors, frequently a previously instituted pneumothorax will drop the lobe down and thus straighten out the upper lobe bronchus sufficiently to permit visualization and biopsy of the tumor. The Papanicolaou smear of the bronchial secretions will also increase the positive diagnoses in those tumors that cannot be visualized. In this connection, it is important to point out that there is no comparison between the cytologic study of ordinary sputum and bronchial secretions. The latter will result in a far higher percentage of correct positive results. However, in this connection a positive smear does not carry the weight of a positive biopsy and should be considered only a link in the chain of diagnosis.

Exploratory thoracotomy, although not a true diagnostic procedure, carries such a minimal risk that it should be mentioned as a diagnostic aid when all other methods have failed. We don't hesitate to do exploratory laparotomies, but for some reason there is a fear on the part of many doctors to recommend an exploratory thoracotomy to a patient. In a small percentage of the cases, this will be necessary to confirm the diagnosis and its application is an important addition to our diagnostic armamentarium.

VII. Differential Diagnosis

In the differential diagnosis it is important to remember that carcinoma of the lung is the great masquerader of chest disease, and this accounts for the lateness of diagnosis. Tuberculosis heads the list in differential diagnosis, and usually can be ruled out easily on the basis of bilateral involvement, positive sputum and occurrence in younger individuals. However, it is most important to realize that a positive sputum does not necessarily rule our carcinoma, as has been so often maintained. Pulmonary tuberculosis may coexist with bronchiogenic carcinoma, and a patient of cancer age, having pain in the chest, dyspnea, weight loss, cough, or bloody sputum, should have a bronchoscopic examination to rule out carcinoma even if the sputum contains tubercle bacilli.

In differentiating carcinomatous from benign lung abscess, the x-ray may be helpful, for with neoplasm there is a greater thickening of the wall, often with scalloping, absence of noteworthy inflammatory changes around the cavity, signs of atelectasis and intrathoracic displacements caused by bronchial obstruction, a lack of change in comparative films, and in the late stages, paralysis of the diaphragm (1). Oftentimes, it is very difficult to make the differentiation, and in fact, in a man past 40 years of age, with an abscess of the lung which cannot otherwise be explained satisfactorily, such a lesion should always be considered of carcinomatous origin until disproved. Tomographic examinations may give a better delineation of the cavity walls, and thus aid in diagnosis.

The x-ray findings of atypical pneumonia are sometimes mistaken for the picture of partial atelectasis resulting from carcinoma of the lung. If there is not prompt improvement in the x-ray picture with adequate medical treatment, then further diagnostic steps should be instituted, including bronchoscopy and cytologic examination of the bronchial secretions to rule out carcinoma. It is too easy to call vague x-ray shadows atypical pneumonia, but with persistent chest symptoms the index of suspicion must be sharpened for neoplasm.

Metastatic carcinomas are always considered in solitary peripheral lung tumors. Routine studies are made for tumors elsewhere, and frequently thoracotomy must be done to establish the diagnosis. Incidentally, it is not amiss to remove solitary metastatic tumors if the primary tumor is resectable.

VIII. Treatment

The only possible hope for a patient with carcinoma of the lung lies in the chance that the diagnosis is early enough to allow complete surgical removal of the lung and the mediastinal lymphatic struc-

tures before metastases have occurred (3). Dr. Evarts Graham performed the first successful pneumonectomy for bronchiogenic carcinoma in 1933, and fortunately the patient, a physician, survived the operation, and when last reported was still alive 14 years later. This has served as an impetus to thoracic surgeons, so that now the accepted treatment is pneumonectomy. This type of malignancy has shown notable resistance to irradiation, and the benefit obtained has been so limited that x-ray treatment has been discarded by most clinics as a curative procedure. External irradiation gives symptomatic relief at best, and is now confined to palliative treatment in inoperable lesions without infection. Its greatest benefit is in relief of pain, but few reported series demonstrate any increase in the life span. Dr. Graham goes so far as to say that he has never seen an authentic five year survival with x-ray treatment alone (3).

As for the other forms of palliative treatment, the nitrogen mustards have been reported by Rhoads (4) to produce transient and incomplete regression in less than 50 per cent of the patients so treated. "Teropteron," the anti-folic acid derivative, has shown no benefit in our hands. Churchill (5) mentions that castration and the use of estrogenically active substances have been explored on the basis of the unequal sex incidence of the disease, but no evidence of benefit has resulted.

As for the survival rate in this disease, a survey reported by Overholt showed that forty-five out of a total of seventy pneumonectomies who at the time of operation showed no evidence of spread, and who survived the operation, lived for variable times, up to 5½ years (6). Twenty died from metastases and five from other causes, making a salvage rate of 64 per cent. Of course, this is in a very selected series, but proves that surgery in ideal cases can effect a substantial five year survival rate. From unselected cases the salvage rate is comparable to that for gastric carcinoma, i.e., 4 to 5 per cent at best. This low rate is due to the fact that at present the operability rate averages about 25 to 30 per cent, and a pneumonectomy mortality rate between 10 and 20 per cent. With earlier diagnosis the operability rate will be increased, and with continued improvement in anesthesiology and surgical techniques, there will be a lower mortality rate.

IX. Conclusion

It is impossible for me to overstress the importance of early diagnosis. The two factors in causing the delay are as follows:

a. The tardiness on the part of the patient in consulting the physician.
b. Delay on the part of the physician in arriving at a correct diagnosis.

The first can be corrected by more widespread and effective education of the general public, increase in the awareness of the gravity of persistent pulmonary symptoms, and the utilization of mass periodic x-ray surveys of the lung. The second can be corrected by increasing the acuity of the physician, increasing his index of suspicion towards this disease, and finally impressing upon him the value of well-established diagnostic procedures such as recognition of the signs and symptoms of the disease, use of various x-ray procedures, the absolute necessity of requesting bronchoscopic assistance, and finally the realization that thoracotomy is a safe procedure. The great majority of cases produce symptoms sufficiently early to permit diagnosis and the institution of successful curative treatment, *provided* the profession does not procrastinate. This is the key to the entire problem.

30 Landing Road

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Modern Medicine
Some Memories and Reflections

Frank J. Doran, M.D., F.A.C.P.

Cleveland, Ohio

I. Introduction

To the Internist, reviewing medicine in its total aspects, and considering future implications of present trends, is part of his nature. An Internist is a physician fitted by a sound and applicable knowledge of the basic sciences; a continuous training in clinical medicine; a familiarity with fields outside his own; and an intellectual approach to study, diagnose, and treat the diseases of the field of Internal Medicine, to which he strictly limits himself, and to integrate, with the knowledge of his own field, that of allied specialties. He must have a vital interest in medicine of the past, of the present and as far as possible of the future. He is interested in not only the diagnoses and therapy of a particular system—but also what may be the effect of that disease and treatment on other systems—on the whole man, and as well the economic and social implications.

During my internship in Cleveland in 1919-20 we had hopes for great strides in medicine as a result of the war. We were still seeing occasional cases of that malignant influenza which began in the morning and were black at night. They were blue—we assumed heart failure and strove to stimulate the heart with digitalis—whiskey—strychnine. It was logical but wrong. As time went on it became apparent that the toxin produced damaged capillaries—fluid flowed into the lung—blood pressure fell—blood was concentrated, with resulting cyanosis. We had medical shock. Had we given treatment for shock many would have lived. This is an example of how far you can depend upon immediate opinion—and the literature. Time may prove it wrong.

I recall pouring quantities of baking soda into diabetic patients in diabetic coma in the pre-insulin days of 1919-20. They all died. Today we realize the patient needs oxidation of glucose, not alkalies, to cure acidosis. But that's what the books were filled with.

I thought, as an intern, that the diagnosis of pernicious anemia was easy. All you had to do was find a nucleated red. Even in 1923, Russell Haden, then in Kansas, said the diagnosis depended on a high volume index and absence of free gastric HCl. Transfusions were the cure as we were sure that the disease was due to destruction of red cells by toxins absorbed from the intestine. We were even giving gentian violet stain in teaspoonful doses to change the intestinal flora. Now we realize the disease was failure to produce cells—the transfusions handicapped cure. But we wrote plenty of heavy dissertations on why we were right. Time took care of a better knowledge. At that time I assisted surgeons bringing home the latest ideas on osteomyelitis, extensive removal of dead bone and closing up tight. I then spent hours dressing the resulting breakdowns, many of which, in the summer, became infested with maggots. It was only a couple of years later that maggot therapy became almost as popular as the present local use of the antibiotic drugs. But it died out as did the enthusiastic use of insulin salve for diabetic gangrene or cod liver oil ointment for burns. We wonder now at the absurdities, but *then*—they seemed plausible. The moral is, don't be misled by the plausible of today. You may be sure a lot of what we swear by now will be an absurdity twenty years from now. A calm search for cause and a firm determination to restrict therapy to attacking cause rather

than symptoms will pay off in personal satisfaction.

II. War: Impact on Medicine

It would be premature to attempt to survey with any finality the progress in medicine which has been made during the past seven years. Much of the data has not been subjected to critical evaluation—more has been written than can be digested at present, and only the faint outlines of the total impact of the war on medicine are visible at the moment.

It can be said that one of the first effects of the war was to shift the emphasis in medical investigation to problems concerning care of the wounded, to prevention and treatment of infectious diseases, and to the effect on physiology of personal reactions to stress. This necessitated a shift from the individualistic type of investigator to that of groups. And these were concerned *more* with new applications of existing knowledge than with the search for fundamental principles.

It can be said that the experimental and clinical development by Florey and associates of Fleming's observations on the antibacterial effects of penicillin was outstanding.

Despite the fact that much has been said about the virtue of sulfonamides in the prevention of all types of infection in wounds during the Second World War, the results of carefully controlled studies on this point show that, while *serious spreading infections* may be controlled by the oral therapy of the sulfonamides in adequate dosage, the development of local wound infection is little influenced by the local or systemic use of these drugs. For example, while advocates for, and against, the effect on wounds were debating, samples of blood of the wounded showed 24 per cent with blood levels of zero or below that deemed necessary for results. Therefore it is evident that reports concerning the efficacy, or lack of efficacy, of the sulfonamides must be taken with a grain of salt.

To date the record shows that but 4.5 per cent of the wounded succumbed. This is to be compared with a death rate of 8.3 per cent in wounded Americans in the First World War, and 10 per cent in the wounded Germans of the first four years of this war. Why is this? Was it the specific therapy or are there other factors? How do we explain the fact that in the Civil War, with no asepsis, no transfusions, no antitoxin, no antisera, no antibiotics, no parenteral therapy, still the death rate of the wounded was only 14.3 per cent, a figure obtained from the Report of the Surgeon General of the United States Army for the year ending June 30, 1900? During the Spanish-American War it was 6 per cent (same ref.); Boer War 8 per cent; Russian-Japanese 5.8 per cent on the Japanese side and 3 per cent on the Russian side.

Contrary to myth and fear, the tendency of wounded men is to get better—not to die; witness 86 per cent surviving in the days before antisepsis. With all our effort and satisfaction we decreased the death rate just 10 per cent. Let us remember *not to say* we saved 96 per cent. The fact is, 86 per cent would have gotten better with no treatment.

On the other hand credit can be taken in the preventive measures. Tetanus controlled. Typhus prevented. D.D.T. controlled the spread of sporadic typhus, serum globulin was found effective in the prevention of measles and infectious hepatitis. In some quarters, pride is felt in the evolution of a vaccine against influenza. I can't get enthusiastic, however. The facts are that in controlled groups of 1000 each: of the vaccinated—2 got the disease; of the unvaccinated only 7 got it. The difference to me is negligible.

Information was obtained concerning prophylactic and suppressive measures against certain types of infection. It was demonstrated that a single dose of sulfadiazine was very effective in eliminating the meningococcus carrier states. But the effects of sulfadiazine in the prophylaxis of beta-hemolytic streptococcus infections were not as happy as in the previous problem. The beta should be eliminated but there developed sulfa-resistant types of streptococci which nevertheless caused outbreaks of pharyngitis, tonsillitis, and

scarlet fever. As a result of these experiences it would follow that the sulfonamides should be used with caution and, until further experience has been gained, their use for the prophylaxis of streptococcus infections in the mass is unjustifiable.

Certain advances in the fields of curative medicine were of signal importance. The development of penicillin therapeutics was spotlighted, notably in staphylococcal and gonococcal infections and surprisingly by its curative effect in syphilis. Quinacrine and chloroquine were found to cure malignant tertian malaria, and hopes for benign tertian are in the offing.

Another interesting development was the discovery of BAL. This compound was demonstrated to be an active therapeutic against both the local and systemic action of arsenical poisonings, notably arsenical dermatitis, arsenical encephalitis, and in the case of the patients overdosed by mapharsen. It may be useful in the blood dyscrasias associated with arsenical therapy but appears useless in alleged arsphenamine jaundice.

Momentous advances in surgical techniques did not stem directly from the War, although during the war definite advances were made in the surgery of certain types of congenital malformations of the heart and great vessels.

It has been fairly easy to outline some of the advances made in the War, but it is much more difficult to assess definitely the impact of the war on the professional development of medical officers and on the education of medical students and doctors. An analysis demonstrates that during the course of a doctor's tour in the Armed Forces, even though he was fortunate enough to be in contact with patients, his professional experience and development was generally limited as compared with that of civilian activity. True, they came in contact with diseases we only read about, and surgical problems due to injuries they had never seen before, and, let us hope, never will see again. Medical officers became alert, and at times almost allergic to the possibility that psychogenic disturbances were at the bottom of all the patient's complaints.

From the educational point of view, it is recognized that it is necesary for physicians to follow their patients from the beginning to the end of their illnesses, if medical, surgical, and nursing skill is to be developed. This was impossible in the theater of war, with the result that physicians knew little of the eventual disposition of their patients.

It seems proper at this point to consider the fact that more than one half of the physicians in this country came under the prolonged control of administrators in the course of their service in the Armed Forces. This exposure came at a time when the doctors in this country stood on the threshhold of a social structure whose protagonists desired, in one -way or another, to organize the medical profession into groups, rather than to permit it to continue in its individualistic course. Now a prolonged experience in the Armed Forces, in which the administration is definitely in the saddle, can't help but leave indelible imprints. This impact may not be apparent at once, as these doctors are dispersed, and at present inarticulate on this point.

It may have been fortuitous for the profession to have sent a large task force down the road, where inefficient administrative control was rampant and, three years later, to have it rejoin the main force as seasoned (if disillusioned) troops. But it is too early to predict the final reactions of doctors to administrative systems of medicine.

Now that the emotionalism of war is over, it is permissible to review some of its exaggerations. We had the Wassermann barbecue; the return to bleeding as something good; blood was easier to get than tomato juice. The result: it has been figured that if every casualty, from a broken toe to profound shock, were to have received all the available pooled blood, each would have drowned in his own fluids and secretions. There were 13,500,000 pints of blood to take care of approximately 300,000 casualties. They needed 33 per cent of the medical profession to take care of 10 per cent of the population on the grounds of emergency casualties, which left 67 per cent of the medical profession to take

care of the civilian needs in which the casualty rate of industry and accidents was 8,000,000 in the nation in 1942 and 36,000,000 from Dec. 7, 1941 to V-J Day. And there is no difference between being hit by a crane or a piece of steel, and the damage inflicted by a bullet or a bomb.

We hanged the German Dr. Schilling for experimenting on concentration camp inmates; and yet we produced infectious hepatitis, and a number of deaths, accidentally, by using a control group of 1000 Navy personnel to check influenza vaccine. This thousand thought they were being protected against a disease, and instead received plasma unfortunately contaminated which would not protect. If this wasn't human experimentation, I don't know what it was.

Dr. John H. Stokes, the outstanding syphilologist in the United States, addressed the Conference on Venereal Disease Needs in Wartime, United States Public Health Service, at Hot Springs in 1942. It has received little or no publicity, in spite of the fact that it contradicted much of the unwarranted claims of public health people in regard to syphilis. I quote: "The past five years, the era of the Wassermann barbecue, and the wholesale application of serological tests to large groups of the *well*, have now shown that the positive test, by any method, is not diagnostic of syphilis in a group of disturbing proportions.

"Wholesale use of screen tests led to confusion. The trouble is as deep as our ignorance of the nature and identity of the syphilitic reagin and this ignorance is profound indeed. The blood test for syphilis has always been recognized as unfit to stand alone; it is a reproach to use it as a sole basis for treatment: it cannot decide, either way, the question of infectiousness ever. There then goes much of its public health significance. The serologic tests for syphilis are not the only ones which disturb. There is reason to suspect that there has long been a serious margin of error in dark field identification of the organism by the inexperienced.

"Foreshortened treatment of syphilis is no novelty. But certain principles should be borne in mind in interpreting all rapid and intensive plans of treatment.

"1. Syphilis cures itself, or comes to rest with little damage, in a percentage of cases probably ranging around 40-50%.

"2. A relatively small amount of treatment is capable of raising the expectancy of cure to an unknown, but considerable degree, maybe as high as 70%

"3. Any system, no system, and even no treatment at all, in syphilis has a running start toward cure then. Therefore the abortive or slower system is directed at a relatively small segment of unpredictable resistant infections.

"4. Any new system must either equal or surpass the curative expectancy noted above.

"5. If the new system equals or surpasses the old it has one more hurdle to make before achieving priority. Primum non nocere—do not injure—must be remembered. Of real importance to the victim are the risks involved and the chance of damage or death from treatment in the case of a disease which with none or very little treatment, gives the victim at the outset a 40-70% chance of escaping serious consequences. Cold evaluation, experience shows, is a secondary, not a primary, characteristic of the clinical mind. From this fact derives the deflation which most enthusiasms for agents and methods gradually undergo. And in some situations a patient shall not be held to a decision as to the propriety of a procedure which may risk his life and health.

"Foreshortened intensive methods sustain a grave reverse in a form of mortality from hemorrhagic encephalopathy based on 4,841 treated cases of 1 in 220 and a morbidity from non-fatal encephalitis of 1 in 160 persons treated. This to be compared with an incidence of encephalopathy by older methods estimated at 1 in 20,000 cases and a total of recorded deaths from mapharsen used in now uncounted hundreds of thousands of cases not to say millions of injections of only 6 reported deaths. The indications are that the death rate will be from 100 to 200 times that of the older, slower, but, when effectively applied, equally effective methods."

It might be well here to touch briefly on another of the events of the recent war. All of our literature has been filled with awesome references to the Atomic Bomb—atomic energy—and mystical references to chain reactions that of themselves may prove to be factors affecting health. Disturbances due to radiation injury are not new. They have been with us since the innovation of x-ray and radium. Many of us exposed to Radiation daily for years, fortunately or not, have developed an indifference to its effects. But I don't see or hear of terrible things resulting, such as many of our returning personnel fear may show up later, because of being in regions where the energy of the atomic bomb was released. Much of the emotionalism and behavior such as using a Geiger counter on a hag of one of the boats destroyed at Bikini is unwarranted and exaggerated.

The destructive force does not differ from previous energy in quality, nor is the nature of the diseases produced any different from the types of radiation sickness or injury we have all experienced. Here are the facts. Warren and Draeger write in the *United States Naval Medical Bulletin,* Sept. 1946 under the title, "Pattern of injuries produced by Atomic Bombs at Hiroshima and Nagasaki": "The classification of the types of injury produced by the explosion of the atomic bomb is the same as that for injuries caused by ordinary high explosives and is extended to include radiation effects. No patient showed injury from induced radioactivity." In other words the radiation effects are the same as those produced by overdosage with x-ray or radium but are not self-renewing due to radioactivity being set up in tissues; and are susceptible to the same therapy we know, used in radiation overdosage.

A Washington news item reports a return to normal marine spawning and life in the Bikini Lagoon with practically no discernible changes; reported by the Smithsonian Institution recently, although it was at first assumed that it might become as sterile as the Dead Sea.

III. Post-War Perspective

You see we are in the same kind of confusion after this war, as memory asserts existed after the first world war. As there were half notions and absurdities then, so, too, are there now. It is our job to separate the real from the fancied progress. Where shall we turn in a situation like this if not to the rediscovery of old Truths, and their re-emphasis in education? One of these is axiomatic. If we are to make progress we must be scientific. Now just what is that? It means that in observing things we look at them as effects of something not immediately apparent—a cause, and then attempt to influence effects— the present problem or case, by getting at the cause; either removing it or preventing it. Up to now because we have obtained some good results, and because all other systems tried have proven, from experience, no better or less good, it has been established that disease is best controlled and health maintained by adhering to three criteria. These are (1) a high grade of personal medical service, (2) scrutinizing, diagnostic judgment, (3) subordinating medication, drugging, and technical manipulation to accurate diagnosis. By these criteria you can recognize Scientific Medicine.

Now with this mental attitude let us consider recent advances in medicine. I think that definite progress can be assumed in the control of the infectious diseases. We are in a position to control the bloodstream invasions, but before which we were helpless. Just as insulin enabled us to combat acidosis successfully, while it did not remove diabetes as a disease, we learned how to enable the diabetic to live a normal life span; so penicillin for the gram-positive infections and streptomycin for the gram-negative invasions will give the sick one an opportunity to combat certain of his infections to a relatively successful termination. And the added good is, as Kolmer states, penicillin seems to be fool proof, a thing unknown in chemotherapy up to this time, a potent drug with little or no hazard. This fact is no justification for its imprudent use in minor self-limited infections. Science demands identification of the organism wherever possible, otherwise the drug will fall into disrepute, because of failure to cure in cases where it

never should have been used. Not so with streptomycin. The drug has a high degree of toxicity and may produce serious hearing defects. Therefore the hazard of the drug must be weighed against the hazard of the disease. Don't be misled by the reports on its use in tuberculosis. Reports and evidence are at hand to show that it does affect the bacillus and the pathology produced. Post mortems have proven this in humans. But it is obvious, to have this proof, the patients must have died. As yet there is not enough reliable evidence to prove cure in tuberculosis.

One of the evils of this help in combatting infections is already appearing. I'll touch on it. Heroic, or unjustifiable, surgical procedures were often prevented only through fear of postoperative infection. The removal of this fear is no justification for convenient cesarean sections, or diagnostic laparotomies.

I am aware of the recent trend to early ambulation of the sick and injured, the reason given being that of preventing thrombosis or thrombophlebitis. The fact that phlebitis and venous thrombosis, admitedly, are most frequent post delivery, and that of 5,742 obstetric cases at the Mayos there were only 20 cases of venous disease, or an incidence of 1 in 300 cases, makes one feel the reason for inflicting a violence on 299, to aid *one,* is not justified. It's a question whether economic pressure for beds has not influenced treatment that is rational and according to the nature of repair. Pathology a long time ago established the reparative time of injured cells. It's about 14 days. And you can't change nature.

I quote from a medical meeting 100 years ago: "We have ever found it difficult to impress upon females the importance and absolute necessity of remaining for a sufficient length of time after confinement in a horizontal position and keeping perfectly quiet. We are satisfied that the practice of getting out of bed too soon after confinement is very general in our community and hence it is, that such a large proportion of our female population suffer with prolapses and procidentia uteri. Sometimes this is attributable to the want of proper precaution on the part of medical advisors but more frequently it is owing to the folly of the patients themselves."

I comment that the modern uterus is just as heavy and the perineum and uterine ligaments just as relaxed now as they were 100 years ago. But there are times when nature cures, in spite of the physician.

A healthy return to unemotional and scientific consideration of medical problems was reflected in the program of papers presented at the 1947 meeting of the A. M. A. To review these would probably be the most rational way to consider what are real medical advances. There wasn't a single paper on vitamin therapy, nor was vitamin therapy, as far as I could determine, considered on any of the many panel discussions.

This brain child of an administration which acted like a doctor was only recalled in two papers presenting the effects of poisoning by vitamin *D* in 50 cases as a result of over enthusiasm for reading *Reader's Digest.* Imagine what we medical people swallowed when, at the time Carlson asked "what is the evidence" and Clendenning revealed a total incidence at Johns Hopkins in a 10 year period of .14% deficiency disease; at that very time, Paul McNutt and Surgeon General Parran said there were 45,000,000 vitamin deficiency cases in the United States.

I think the greatest interest was seen in the use of new palliative drugs in combatting neoplastic processes of the blood-forming system. You will hear of those drugs. Urethane—nitrogen mustards—and stilbamidine. No cures but encouraging effects on the abnormal cells of leukemia (chronic; nothing significant in the acute) — Hodgkin's — and multiple myeloma. They are not cures and they do not substitute for the older methods yet.

The same with thiouracil. Like Lugol's it seems to be an agent giving us better control over the toxic thyroid, preventing the catastrophic crisis, from which none return, but it does not replace iodine or surgery. It does allow one to procrastinate safely for a while. Again not a cure.

Hematology. There have been recent advances in the knowledge of blood disorders

that have led to improvements in the management of several serious and puzzling diseases.

In primary anemia a factor to stimulate red cell production was found in liver and used. Cases arise of inability to take liver; or other primary anemias, sprue and simple nutritional macrocytic anemia, did not respond to usual liver doses. Spies and others demonstrated folic acid effective by mouth in stimulating the bone marrow. It does not, however, prevent the spinal cord changes present in pernicious anemia. Therefore a help but in pernicious anemia not a substitute for liver.

Early recognition of the Rhesus factor present in 85 per cent of humans explained many transfusion reactions, although of the same group, and later explained the occurrence of that peculiar disease of the newborn, icterus neonatorum or bleeding and hemolytic tendency, three phases of which, mild—anemia of the new born; moderate—icterus gravis neonatorum; and severe—hydrops fetalis, are all now classes of erythroblastosis fetalis. This recognition led to a more satisfactory control.

With the exception of those bleeding diseases attributable to deficiency in prothrombin, our present knowledge and treatment of hemorrhagic disorders are still in a highly unsatisfactory state. In the exceptions mentioned, giving vitamin K and bile salts solves the problem. Oddly enough this disease, prothrombin deficiency, is deliberately caused by dicumarol and other anticoaagulants in thrombophlebitis and posttraumatic states to prevent possible pulmonary embolism. I insist this is still hazardous, highly experimental, and has no place in the general hospital as yet, if ever. I heard one man in a panel discussion say that at the Mayo Clinic they were using it at the present time in cases of coronary thrombosis until they had 100 cases treated, to compare them with 100 coronary cases treated without it. I don't think that I'd want my brother treated that way, as his coronary attack is the only one he will have, and time may prove the anticoagulant is not a good thing. It is still experimental and we have no right to experiment on private patients. I called attention to the infrequency of pulmonary embolism and venous disease. I think reports of high incidence ignore the countless cases of venous thrombosis which never come to an institution or even to a doctor and therefore forget that the nature of the disease is not to spread but to get beter.

In the last 20 years we are forgetting the principle advocated by Osler and Flint which picked medicine out of the era of shotgun therapeusis to sound therapy. Osler laid down, then, that a cardinal principle in the therapeutics of a disease was a knowledge of its natural history; that we had to know the course of a malady left to Nature before we could appreciate the action of medicines given for its cure. At the time that Flint graduated no one would have dared to treat a case of pneumonia from its beginning to its termination without a drop of medicine. The man who would have attempted it would have been looked upon as in the highest degree worthy of blame and censure, and certainly in private practice would not have had the confidence of the family for 24 hours. Osler's rational use of drugs was much too far advanced for staid Philadelphia. One can imagine a naturally conservative city—the Mecca of medicine—to which the eloquent Dr. Wood was extolling the value of drugs and the equally eloquent Pepper recommending a dozen different drugs in the treatment of individual diseases, shocked into insensibility by having a young professor of medicine, recently come into their midst, go through the wards and discourage symptomatic drugging. But in reality Osler was a very good therapeutist as the interns realized and used drugs not empirically but scientifically and his teaching laid great stress upon the general management of disease.

Transfusions of whole blood or plasma globulin is still the only resort in the exacerbations of the hemophiliac.

In the diseases characterized by decrease in platelets, there has been no improvement over the transfusions and splenectomy.

Some bleeding is due to local capillary abnormalities, increased permeability due to deficiency disease, toxic substances and anaphylaxis, with no abnormal blood

changes but a positive tourniquet test. These states are occasionally referred to as pseudohemophilia. Here our only hope is to treat symptomatically. The recently much publicized vitamin P-like substance—rutin, has not been effective in controlling abnormal permeability in any of these diseases. Furthermore, it appears to be of little benefit in preventing or controlling hemorrhages in high blood pressure patients, although it has been widely publicized.

Leukemia, first discovered 100 years ago as a clinical entity, still defies our efforts to avert the universally fatal outcome, or even to prolong the life of its victims. Radioactive isotopes as yet are not developed to the point where they will be selectively deposited in and will selectively destroy leukemic cells. Such a development might well provide, for the first time, a really satisfactory treatment for leukemia. It is this desideratum we seek likewise for the chemotherapeutic agents methyl-*bis* and urethane.

Much publicity has recently been given to the growing practice of surgery of the vagus nerve in controlling gastric acidity and treating peptic ulcer. This seems to be a case of ignoring the principle that the hazard of the treatment must not be greater than the hazard of the disease. My opinion on it coincides with that of Dr. Frank Lahey: "To advise, or to do vagotomy for the cure of peptic ulcer, prior to at least three months of medical treatment, followed by sub-total gastrectomy, is nothing short of malpractice." Therefore surgeons are assuming a grave responsibility in premature publication of results of operations that properly cannot be evaluated for at least 5-10 years. This is a warning not to accept, too readily, promises based on theory and experimental surgery.

We have always looked upon cirrhosis of the liver as a terminal picture of misspent life. In my own experience most of the cases of cirrhosis occurred in females who never took a drink in their lifetimes. But it was a terminal picture. Today the outlook is better. Although 10 years ago Bollman proved that to produce cirrhosis in a dog, he had to take the human equivalent of 1½ quarts of liquor a day and that his cirhosis got better when he didn't get the liquor, only now is it being admitted that alcohol is only indirectly or not at all involved in its production. It seems to be a deficiency disease, and although there is not enough space, facts can be cited which seem to demonstrate it.

One of my friends is quite enthusiastic in his results at Bellevue in New York from the intravenous use of especially prepared liver extract. At any rate if we can prolong life in cirrhosis 5-10 years, something has been accomplished.

About cancer, let me express a private opinion which I hope will not startle anybody. We have before us a shameful spectacle in the cancer prevention propaganda. It is admitted without exception that we have absolutely no knowledge of the real cause of cancer and that we grope blindly in all our methods of treatment. We employ the knife and radium and x-rays because we obtain some temporary and a few permanent results and because we know no better. Metastatic cancer is incurable by any method of therapy, surgery, x-ray or radium. Still that does not deter propagandists and, to our shame be it said, also medical propagandists from literally frightening people, even schoolchildren, out of their wits and making vain promises and arousing false hopes which are so often followed by tragic awakening. I venture the opinion that whatever the motive, science is not served thereby. Why not tell people that of all the human beings living in the world today, 90 per cent will never develop cancer anywhere in the body. And of those who do, one-half of them will occur on the skin or orificial mucous membrane and are 100 per cent curable because they are accessible to observation and uncomplicated removal.

I won't bore the reader with present attitudes on hearts except this—the effects of cigarette smoking on cardiacs. For a long time we have been trying to cure the vices of smoking and drinking through fear of disease. Well, eight years ago, Ivy provided the only scientific data on the effect of cigarette smoking on acidity in ulcer patients. It not only didn't increase

acidity, it actually decreased free HCl. Somebody, now, will advise ulcer patients to smoke cigarettes. This year Dr. Levy and his associates observed the cardiac output, rate and blood pressure, in other words, work in normals and cardiacs with cigarettes and denicotinized cigarettes. Conclusions: "The results indicate that variations in response are *no greater* in cardiacs than in normal patients; that in both groups the reactions are minimal. There is no difference between the effects of ordinary cigarettes and denicotinized cigarettes. It appears, then, that patients with heart disease including coronary thrombosis and angina pectoris, except those who show abnormal sensitivity to nicotine, may be permitted to smoke in moderation."

These, then, are the facts on modern drugs and methods, about which so much has been written, and from which is expected so much. A little retrospection to the First post-war enthusiasms, ideas, and promises will sober the over enthusiastic and protect the credulous. Insulin did not dispense with diet. Lugol's did not outmode surgery. Liver did not cure pernicious anemia.

So today, we will be helped, and not later be disillusioned, if we accept modern trends as adjuvants or methods to help, not to substitute for the older conservative methods, and perhaps solve the problem of those cases resistant to the well-tried therapy.

Now in closing, I should like to touch shortly on the modern trend to change the system of scientific medicine, which appeals to many well-intentioned but misled sociologists, politicians, philanthropists and writers, particularly newspaper editors.

For all their effectiveness, modern medical techniques are dangerous and medical knowledge is of little avail unless applied by men of wisdom and integrity. When medical cure was simple and ineffective, it was also harmless, and the fine exercise of judgment required of the present-day physician was less frequently required. But the medical profession possesses all the virtues and all the faults of human nature. In addition to the wise and honest doctors and scientists, we have our full share of voluble snap diagnosticians and researchers who are long on theory and short on judgment and are as numerous as surgeons whose concern for the patient fades if convalescence is stormy.

It follows that any system of extending medical care to all people, instead of *just to those who are sick*, is ignoring the fact that the doctor of quality is limited in number. To give them more work is to adulterate the quality. The objection is raised that the public will not wait and will set up its own system of extended medical care. To this I say: Let them light the fire: they will be badly burned and learn their lesson. Some well-intentioned, well-financed group will establish a medical care plan and due to a dearth of good men will place it under the care of poorly qualified physicians. Patients will be cared for by men with pet theories "which were formerly inflicted on relatively small groups of private patients or by surgeons long on speed and short on incisions." But these patients will not be saved by drifting to another doctor. They will have prepaid their money over years, will return for amends and bad news will follow. And then only will the backers come to realize that although expenses have been met, they are operating under a deficit, a deficit peculiar to medical undertakings—loss of public confidence, deterioration of scientific medicine, and a return to medical charlatanism, and the influence of sects and cults.

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Fever Therapy Makes Penicillin More Useful Against Syphilis

Artificially produced fever increases the effectiveness of the seven and a half day penicillin treatment for syphilis to more than 80 per cent, a substantial improvement over both penicillin alone and penicillin and mapharsen in combination for the same length of time.

EDITORIALS

A Junior Bomb Already in Operation

Meigs regards the increasing incidence of endometriosis as a social phenomenon foreshadowing a decline in our civilization. Speaking before the American College of Surgeons on October 20, in Los Angeles, he declared that the ailment pointed to the eventual displacement in social dominance of healthy and intelligent people by the weak and unintelligent but fecund class. This threat overshadows the problems of the ailment in the individual patient. Early marriage, subsidized in one way or another if need be, and certain reforms in our society, are advocated by Meigs.

The Harvard gynecologist believes that "the most necessary class in society" can be increased and that this educated and intelligent class could then, with good luck, defend itself successfully against the "occasional genius" from the other class. This seems to be an admission that it is not the steady, dependable, mediocre people who are the source of genius and to represent a conviction that geniuses are not needed and can be dispensed with. Meigs's conception of genius, however, is limited, for in his mind it seems to connote, chiefly, the Hitlers, Mussolinis and Stalins.

The right sort of genius is badly needed and can not be dispensed with, no matter how dubious its source, if human society is to further mature.

There is some confusion here, yet to be resolved.

We suspect that Meigs inclines strongly to the eugenic doctrine of respectability as the chief criterion of value in men.

At any rate, endometriosis poses a problem for us approaching the Atom Bomb in seriousness.

Home Medical Care

New York's municipal hospital system is creating hundreds of beds by the rational expedient of discharging patients for home care who no longer need specialized medical care in the hospitals. The City will provide the home care and has made appropriations for it.

Montefiore Hospital set the example for the City in 1947, reducing the cost per patient per day to the hospital from $8.75 to $2.25.

The City finances its plan by means of its increased subway fare. Unfortunately, the pressure on private hospital beds can not be relieved by a similar measure, since the staffs of such hospitals are determined to treat all their non-ambulant cases under one roof—that of the hospital. This has been the situation for many years, representing a complete revolution since the days when most patients were treated in their homes and when eminent consultants were available in the home as well as in the hospital. The middle-class home of the present owes its well known fall from grace largely to the anomalous system now prevailing for which the medical profession is respnosible. It is part of the mess which characterizes all the activities of the present era, and is seemingly not susceptible of unscrambling.

No Dogma Is Sacred

One of our more sacred dogmas has to do with the alleged danger to the middle ear of forcible nose blowing with compressed nostrils and closed mouth. Now we are being told by the aviation medical services that air compression of this sort does not account for most middle ear infections. Such infections are alleged to be due to primary disease in the eustachian tube leading to its obstruction with a consequent

vacuum in the middle ear, the vacuum inviting invasion.

No dogma is sacred any more.

The Eugenic Snob

Professor Barrett Wendell is alleged to have told one of his Harvard classes that the qualifications of a true Bostonian were "a share in the Athenaeum, a lot at Mount Auburn and a relative in the insane asylum."

Something of the same sort is needed to make a good eugenist. We suspect that many of the leading lights in this field have had their interest in the subject aroused by their own bizarre relatives and ancestry. They are often themselves, we fancy, carriers of sinister genes and sterilization should probably begin with them. To be wholly on the safe side we should perhaps liquidate all eugenists.

The rational eugenist knows, if he knows anything, that the eugenic program really gets nowhere unless carriers as well as the unfit themselves are taken in hand.

We know what the eugenists under the Hitler régime were like. Indeed, the whole eugenic program since that ineffable dispensation has been under a cloud. Unlimited power always corrupts and no group of eugenists can ever again be trusted with it.

✚

GENERAL PRACTICE

MIRABILE DICTU!

Wonderful to relate, the *New York Times* (November 7, 1948) has attained astonishing wisdom. Behold the evidence in the last sentence of the appended editorial. We salute the writer and the publication for their astute recognition of a social necessity and for their civilized acceptance of one desirable trend of the times.

HOSPITAL SERVICE

The tradition of the seventeenth century, according to which a voluntary hospital is a charitable institution supported largely by gifts from the philanthropically inclined, is not dead. The remnant of it that lives was discussed by Dr. Joseph G. Norby in the presidential address he delivered before the American Hospital Association.

Only in their free clinics are hospitals allowed by law to practice medicine. This is surely an anomaly. There is no technical reason why a sick person should not walk into any hospital of his choice and ask for staff service in a private or semi-private room for which he is willing to pay a reasonable price, but the law forbids. Though the sick are turning more and more to hospitals, largely because first-class medicine cannot always be practiced in a private office for lack of the proper diagnostic and therapeutic aids, the law remains.

Hospitals need more certain sources of revenue than donations from the warm-hearted. Dr. Norby is probaly right in thinking that industry is willing to contribute an even greater share to the support of hospitals than it does, and by industry he means not only employers but employes. The labor unions, too, have a large stake in good medicine and are likely to follow the example of the coal mines in insisting that more attention be paid to the medical needs of sick and injured workers. Blue Cross plans have been a financial boon to hospitals, but there is still opposition in some medical circles to their extension, so that they may include medical care in hospitals by staff physicians. Much of this opposition might disappear if hospitals conducted themselves as public institutions to which any qualified physician could bring his patients.

✚

Progress in the Fight Against The "White Plague"

The largest single health campaign ever undertaken is now in progress under the technical direction of the World Health Organization. Cooperating in the program are the International Children's Emergency Fund, the Scandinavian Red Cross societies, and the local governments. For the first time in history, tuberculosis, the white plague, is being combatted on an international scale by the coordinated efforts of doctors, nurses, and health workers, backed by superior laboratory and other technical work and financed by a budget of almost 5 million dollars.

This concerted drive against TB is in force now in Czechoslovakia, Yugoslavia, Poland, Hungary, Finland, and other devastated countries of Europe and is about to be extended into Germany. It is in operation in Asia, where China and India are participating, and the plan will soon be extended to North Africa.

The campaign is a preventive one. A principal aim is to make children safe from tuberculosis by vaccinating them with BCG.

CONTEMPORARY PROGRESS

UROLOGY

The Incidence and Extent of Hydronephrosis in Prostatic Obstruction

H. L. Kretschmer and F. H. Squire (*Journal of Urology*, 60:1, July 1948) present a study of the incidence of hydronephrosis in 408 cases of prostatic obstruction. These cases are divided into two groups: 186 cases studied in 1933 to 1937, and 222 cases studied in 1945 to 1947. In all cases the diagnosis of hydronephrosis was made by intravenous urography. In the earlier group, the average duration of symptoms before the patient sought medical advice was 60.5 months; in the second group 43 months, a difference of 17 months, or nearly a year and a half. In the first group, there were 80 cases with evidence of hydronephrosis and hydroureters, an incidence of 33.43 per cent. The incidence of hydronephrosis was, therefore, definitely less in the group in which the duration of symptoms was shorter. In the first group there were 21 cases of carcinoma, and in the second group 24 cases of carcinoma, an incidence of just over 12 per cent in both groups. This incidence of carcinoma is lower than in any other published series of cases. Hydronephrosis was present in 14 of the 21 cases of carcinoma in the first group and in 10 of the 24 cases of carcinoma in the second group. In addition to dilatation of the ureters, changes in the course of the ureters—lateral displacement, angulation and elevation of ureters at the point of their entrance into the bladder—were found in 86 cases in the combined series. Such changes may be of diagnostic value. Bladder changes due to obstruction—diverticula, cellules and stones—occurred more frequently in the first than in the second group. As the incidence and the extent of hydronephrosis and the incidence of coexistent bladder disease are in direct relationship to the duration of symptoms in prostatic obstruction, an educational campaign urging patients to seek early relief for such symptoms is justified.

COMMENT

Any obstruction to the ureters, if long continued, must produce hydro-ureter with displacement, angulation, elevation, etc. The wide variety of prostatic enlargements is a fertile soil in which such changes occur. As the pelvis of the kidney is only a collecting pouch of the ureter it must share antecedently any such changes in the ureter. These authors are to be congratulated upon having established the diagnosis by x-ray pictures.

V.C.P.

Primary Carcinoma of the Seminal Vesicle

E. M. Gee (*British Journal of Urology*, 20:72, June 1948) reports 2 cases of primary carcinoma of the seminal vesicle, seen at the Toronto General Hospital. The first case was the only case of the kind found in autopsy records of the Hospital between 1906 and 1946; the second case was seen at the Hospital in 1947. A review of the literature shows 21 cases of primary carcinoma of the seminal vesicle reported between the years 1883 and 1943; the author's cases bring the total to 23 cases reported. In many of the reported cases, the diagnosis was not made during life; in several cases a palpable mass was found by rectal examination; in some cystoscopy showed signs of obstruction and secondary invasion. In the author's first case "a hardening" over the right lobe of the prostate "suspicious of carcinoma" was noted in a routine physical examination two years before the patient's admission to the hospital; at that time he had no symptoms; repeated examinations did not confirm the diagnosis of carcinoma, but showed pros-

tatic calculi. The first symptoms noted by the patient were blood in the urine and pain in the back; x-ray examination showed destructive lesions in the thoracic vertebrae and ninth rib; pathological fracture of the spine occurred, for which the patient was treated; death occurred nearly three months after his admission to the hospital, after "the usual sequence" of cystitis, pyelonephritis and uremia. At autopsy primary carcinoma of the seminal vesicles was found without evidence of invasion of the prostate; the bladder wall around the ureteral opening was involved; most of the right and part of the left seminal vesicle were destroyed. In the second case the first symptom noted by the patient was pain in the lower abdomen pasing downward over the pelvis into the external genitalia, diagnosed as seminal vesiculitis. When admitted to the hospital four months later the patient had lost weight. At that time, the prostate felt normal on rectal examination but there was a pyriform mass just above the prostate on the left side where the seminal vesicle should begin. Treatment with sulfonamides, penicillin and streptomycin (because of the possibility of tuberculosis) had no effect. An exploratory operation showed a hard nodular mass in the region of the left seminal vesicle that had invaded the pelvic wall and could not be removed. Biopsy showed carcinoma of a highly anaplastic type. The patient died six weeks later. The author suggests that even if there are no symptoms and a small suspicious mass is found in the prostate or seminal vesicle exposure through the perineum and biopsy by frozen section should be done, with radical excision of the lesion if malignant. In the second case the tumor was probably inoperable when the patient was first admitted to the hospital.

COMMENT

Here we have a rare lesion, twenty-one cases reported in 60 years! In one of the author's cases both vesicles were involved but not the prostate, while the bladder wall around the ureters was involved. One would feel that mere proximity of the lesion to the prostate would have led to the latter's inclusion.

V.C.P.

Cryptorchism

L. G. Lewis (*Journal of Urology*, 60:345, Aug. 1948) presents a review of the literature on cryptorchism and concludes from this and from his own experience that hormone therapy can bring about descent of the testes by activating the normal mechanism of descent if there is no anatomical or pathological condition that prevents this descent. Hormone therapy should not be employed until the boy approaches puberty, one or two years before the normal expected onset of puberty. At that time, the author considers that antuitrin-S in a dosage of 500 rat units three times a week should be given up to a total dosage of 30,000 rat units. If this does not result in descent of the undescended testis (or testes), operation should be done without delay. Treatment for cryptorchism before puberty is indicated in order to preserve the spermatogenic function of the testis. In the author's experience the Torek operation, a

traction suture method, has given excellent results in the surgical treatment of cryptorchism. Preservation of the internal spermatic blood vessels is necessary for spermatogenesis following orchiopexy. If for any reason the testes cannot be placed in the scrotum, they should be allowed to remain in the abdomen when the cryptorchism is bilateral, to continue their interstitial function. While it is true that testicular tumors develop more commonly in undescended testes, the incidence of testicular tumors in such testes is not sufficiently high, in the author's opinion, to justify removal of the undescended testis in unilateral cryptorchism.

COMMENT

The most impressive fact brought out in this paper is that hormone treatment about puberty may cause descent. The Torek operation has much to commend it as it fastens the testis to the fascia of the thigh making it independent of scrotal structures. These testes are usually anatomically imperfect and must contain much embryonal tissue which leads to carcinoma. Personally I favor removal if the Torek operation fails. V.C.P.

Urethrography: A Diagnostic Aid in Diseases of the Lower Urinary Tract

W. E. Goodyear and asociates (*Southern Medical Journal,* 41:487, June 1948) describe a method of urethrography using 27 per cent sodium iodide in peanut oil as an opaque medium; the x-ray exposure is made while the last few cubic centimeters of this medium are being introduced; only one x-ray exposure is required. This method has been found superior to other methods of clinical investigation in urethral stricture and in trauma involving the urethra. Urethrography has also been found of value in the study of prostatic hypertrophy and prostatitis; the diagnosis of carcinoma of the prostate cannot be definitely made by the urethrogram. Following prostatic surgery, urethrography is of value to determine the results and indicate the prognosis for normal urinary function without the pain and trauma of endoscopy or sounding.

COMMENT

A very interesting article in that the method described includes all the ordinary lesions of the urethra and prostate. V.P.

Streptomycin in Treatment of Tuberculosis and Mixed Infections of the Genito-Urinary Organs

F. R. Redewill and J. E. Potter (*Urologic and Cutaneous Review,* 52:259, May 1948) report the treatment of tuberculosis of the genito-urinary tract with streptomycin combined in most instances with penicillin and promizole. The dosage of streptomycin was 1 Gm. daily, given in two doses during the day. In tuberculosis of the bladder, iontophoresis, quartz light and supplementary vitamins A and E were also employed. The protein intake of the diet was increased if it had been low. In nontuberculous mixed infections of the genito-urinary tract penicillin is effective against most coccal infections, streptomycin against gram-negative rod as well as coccal infections. In the treatment of mixed infections, combinations of penicillin and promizole, streptomycin and promizole, or streptomycin, penicillin and promizole were used, according to the nature of the infection. Before and during treatment the potency of penicillin and streptomycin against the infecting organism must be determined repeatedly in order to discover any "fastness" of the organism against either antibiotic. In 22 cases of genito-urinary tuberculosis treated there were 15 apparently cured, 6 improved and 2 not improved. In the mixed infections, cure was obtained in 19 of 25 cases of pyelitis and cystitis, in 17 cases of acute cystitis and 37 cases of acute urethritis, in 16 of 17 cases of chronic urethritis and in 18 of 23 cases of chronic prostatitis.

COMMENT

It is very instructive to note that combinations and sequences of these substances are being developed. Also that frequent tests during treatment for fastness of the organism are employed. This brings the matter down to an accurate basis. V.C.P.

OBSTETRICS

The Fate of Living Viable Babies in Extrauterine Pregnancies

M. Suter and C. Wichser (*American Journal of Obstetrics and Gynecology*, 55:489, March 1948) report 4 cases of extrauterine pregnancy with living viable babies recently seen at the Charity Hospital of New Orleans. All of these infants were delivered alive, but 2 died within a few minutes, and one within twenty-four hours. All but one of these children showed gross deformities at birth. The one child who was apparently normal died within a few minutes. One of the infants, in spite of gross deformity, lived and was doing well at the last follow-up five months after birth. All the mothers recovered. A tabulation of 41 other cases of extrauterine pregnancy reported in literature in which living viable babies were delivered is presented. In these cases a specific statement was made as to the development of 31 infants; 12, or 38.7 per cent, were deformed, and 10, or 24.3 per cent, died before the eighth day. From a review of the literature, the authors conclude that only about one fourth of extrauterine pregnancies in which diagnosis is made after the fifth month of gestation will result in viable, living infants; about one third of such living infants will have some major or minor deformity, including deformities incompatible with life; approximately one-half of such living, viable infants will survive eight days or more.

COMMENT

It is a well known fact that the salvage of living healthy babies from extra-uterine pregnancies is very small. The hazards for the fetus are numerous and frequently of grave import. The authors conclude from a review of the literature and their own experience that only about 25 per cent of extrauterine pregnancies in which the diagnosis is made after the fifth month of gestation will result in viable, living infants; about one-third of such living infants will have some major or minor congenital deformity; and approximately one half of such living, viable infants will survive 8 days or more. This is about what our experience has been and yet we can recall two perfectly well and healthy babies that lived and were a joy and delight to the parents and of considerable satisfaction to the doctor. Be careful of your prognosis in abdominal pregnancy—both for mother and baby. H.B.M.

Rubella in Pregnancy as an Etiological Factor in Stillbirth

Charles Swan (*Lancet*, 1:744, May 15, 1948) reports a study of 760 stillbirths occurring in South Australia. A history of rubella during pregnancy was reported by the mother in 16 cases (in one case this diagnosis was doubtful); in 13 of these 16 cases the rubella occurred in the first four months of pregnancy, i. e., in the so-called "critical period" for the production of congenital abnormalities. In half of these 16 cases no cause for the stillbirth could be determined by the attending physician. In the series of 760 pregnancies other infectious diseases were of rare occurrence and none showed the predominance in the early months of pregnancy characteristic of rubella. Since the stillbirth, 10 of the 16 mothers have had one or more children, all of whom are living and well. These findings suggest that rubella may be an etiological factor in stillbirth by causing damage to the embryo early in pregnancy.

COMMENT

In 760 stillbirths reported by the author, a history of rubella during pregnancy was reported in 16 cases; in 13 of these cases the rubella occurred during the first four months of pregnancy. This is the so-called "critical period" for the production of congenital abnormalities. Other reports confirm these observations. The nature of the toxic agent and the modus operandi is not very clear. We have had no personal experience with rubella complicating pregnancy. It must be very rare in greater New York. H.B.M.

Obstetrics in the Small General Hospital

C. E. Conner (*Surgery, Gynecology and Obstetrics*, 86:499, April 1948) reports 2,500 deliveries in two general hospitals in Wenatchee, Washington in 1944, 1945 and 1946. One of these hospitals has a

capacity of 55 beds and 20 bassinets, and the other 75 beds and 20 bassinets. The majority of deliveries were attended by general practitioners of the community. There were 16 pairs of twins delivered in this series. There were 5 maternal deaths, a maternal death rate of 0.20 per cent, which compares favorably with the maternal mortality rate of the United States for 1940 (0.376 per cent) and of the State of Washington for the same year (0.306 per cent). The causes of death in these 5 cases were shock and hemorrhage following vaginal delivery of a placenta previa, acute yellow atrophy of the liver, severe rheumatic endocarditis, diabetes mellitus, and ruptured myocardium in the first stage of labor. There were no deaths or serious complications from puerperal sepsis or toxemia. These results "speak well" for the care that a general practitioner and a general hospital can give an obstetrical patient. The infant mortality was 3.28 per cent (82 deaths), also relatively low, though less strikingly so than the maternal mortality rate. There were 28 stillbirths; of the neonatal deaths, 24 were due to prematurity. There were 5 cases of pre-eclampsia, in 3 of which cesarean section was done, and 3 cases of eclampsia (all with antepartum convulsions), in one of which delivery was by cesarean section. In the case in which death was due to acute yellow atrophy of the liver, the patient had had hyperemesis gravidarum during most of her pregnancy, and was first seen at the hospital when in labor. Of 18 cases of placenta previa, delivery was by cesarean section in 10 cases; of the 8 patients delivered vaginally, one died, but the infant lived. In the entire series of 2,500 deliveries, 74 were by cesarean section; the chief indication for this operation was cephalopelvic disproportion, in 49.3 per cent of the cases. There were no maternal deaths in this group; the infant mortality was 2 per cent. Low cervical section was done in only 20 of these 74 cases; only obstetrical specialists did the low cervical operation; classical cesarean sections were done by general practitioners. There were no cases of peritonitis following cesarean section although some operations were done more than twenty-four hours after rupture of the membranes; the use of penicillin or the sulfonamides is probably responsible for this result in some of the cases. Although the results in this series of cesarean sections are good, the author is of the opinion that low cervical section should be more frequently employed.

Comment

Obstetrics in a small community hospital can be just as good as in a large institution. This is particularly true if the group of general practitioners doing most of the work are conscientious observers and call for early consultation in their problem cases. Early consultation never lessened any physician's standing—in fact it generally enhances it. The report by Dr. Conner is worthy of emulation by many a small obsetric hospital that is doing excellent obstetric work. The specialists working in big hospitals do not deserve all the credit for our present day low maternity rates. The general practitioner, who delivers more than half of the babies born each year, deserves some credit. ***H.B.M.***

A Study of the Use of Penicillin in Premature Rupture of the Membranes

J. E. Woltz and T. S. Stashak (*American Journal of Obstetrics and Gynecology,* 55:859, May 1948) report a study of 57 patients with premature rupture of the membranes. In all these cases the rupture of the "bag of waters" had occurred at home and uterine contractions had not begun before admision to the hospital; none of the patients were examined vaginally. Penicillin in a dosage of 12,500 units every three hours given intramuscularly was employed in 29 of these women from the time of admission until delivery; 28 were not given any penicillin. One woman in each group stopped leaking fluid, did not go into labor, and was discharged from the hospital. All the other patients went into labor spontaneously. At the time of delivery cultures from the cervix were made in 24 of the 29 patients given penicillin and in 21 of the 28 untreated controls. Pathogenic organisms were present in the cervices of both groups; staphylococci predominated in the untreated group

and the diphtheroid bacillus and *B. coli* in the penicillin-treated group; gonococci were found in one patient in the untreated group. Only 2 of the patients given penicillin (6.9 per cent) showed puerperal morbidity (a rise in temperature to 100.4°F. on any two days exclusive of the first twenty-four hours after delivery); 6, or 21.4 per cent of the untreated patients, showed puerperal morbidity. The latent period, i.e., the period between the rupture of the membranes and the onset of labor, was not affected by the administration of penicillin, indicating that penicillin has little, if any, oxytocic effect on the uterus at or near term. All the morbidities in both groups occurred in patients in whom the latent period exceeded twenty hours. The fact that the administration of penicillin definitely reduced the incidence of puerperal morbidity in cases of premature rupture of the membranes indicates that it should be employed routinely in cases of this type.

Comment

This report of only 57 patients with ruptured membranes where penicillin was used prophylactically is, of course, too small to be conclusive; yet we know, from a very much larger series, that such a routine is valuable and does "cut down" the morbidity rate. The longer the membranes are ruptured the more prophylaxis is needed. However, I am not so "anxious about ruptured membranes" in my private cases as many men seem to be. On the other hand, ruptured membranes for long periods of time (18-36 hours) are a potential, if not a real, source of infection and we should therefore employ chemotherapy and/or the antibiotics routinely in such cases. There is no harm and it may prevent a serious infection. Prevention is always in order. ***H.B.M.***

ARTERIAL HYPERTENSION

—Concluded from page 524

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Medical BOOK NEWS

Edited by
ANDREW M. BABEY, M.D.

All books for review and communications concerning Book News should be addressed to the Editor of this department, 1313 Bedford Avenue, Brooklyn 16, N. Y. When books are sent to us with requests for review, selections for that purpose are promptly made.

S. WEIR MITCHELL
1830 - 1914

Classical Quotations

● In rare cases, the first pain is said to be an ache of the foot; but in the mass of instances, and soon or late in nearly all the pain is of a burning character. "It is the pain of a burn"; "the pain of mustard"; "of intense sunburn"; at least these are the phrases used to describe it, and certainly the character of the suffering is so well marked as to be clinically distinctive.

S. WEIR MITCHELL
on a Rare Vaso-Motor Neurosis of the Extremities. *Am. J. M. Sci.* 1878, LXXVI, 1-36.

Gynecological Pathology

Gynecological and Obstetrical Pathology. With Clinical and Endocrine Relations. By Emil Novak, M.D. 2nd Edition. Philadelphia, W. B. Saunders Co., [c. 1947]. 8vo. 570 pages, illustrated. Cloth, $7.50.

This second edition shows the same thoroughness that this excellent teacher always gives in his presentations.

The purpose, as described in the preface of the first edition—"the work . . . represents the author's concept of the composite needs of the student, practitioner, specialist, and pathologist in his particular field"—has been closely adhered to, and the result is a practical, clear, authoritative compilation of facts.

This revision adds many details and often completes the picture which in some instances would never have been possible without revision.

The book is highly recommended.

CHARLES H. LOUGHRAN

More About Nicholas Culpeper

The Affairs of Nicholas Culpeper. By Mabel L. Tyrrell. Philadelphia, Macrae-Smith Co., [c. 1946]. 8vo. 352 pages. Cloth, $2.50.

This is rather an odd novel built around the facts and fancies relating to an herbalist of the 17th century. The hero being a very able person, appears in the book as being more against than for things. He is against the "regular profession," but, withal he is for the poor and nearly destroys himself giving his strength for them, with little regard for the rich, who would welcome his services. A very odd love affair and its tragic ending, followed by a very satisfying marriage, with some intimations of life at that period, make up a book, which can be read with some enjoyment.

WALTER D. LUDLUM

Eye Diseases

Gifford's Textbook of Opthalmology. By Francis H. Adler, M.D. 4th Edition. Philadelphia, W. B. Saunders Co., [c. 1947]. 8vo. 512 pages, illustrated. Cloth, $6.00.

The fourth edition of Gifford's Textbook of Ophthalmology edited by Francis H. Adler, comes up to the high standards of previous editions. It has been brought up-to-date, without materially increasing its thickness, by the addition of new material and condensation of the sections on refraction and operations. Emphasis is placed on medical and neurological aspects of ophthalmology and on those diseases of the eye with which the general practitioner is most often concerned.

JOHN N. EVANS

Dermatology

Diseases of the Skin. By Oliver S. Ormsby, M.D. & Hamilton Montgomery, M.D. 7th edition. Philadelphia, Lea & Febiger, [c. 1948]. 8vo. 1,462 pages, illustrated. Cloth, $18.00.

In this new edition the authors have brought up to date their excellent book. The revisions are particularly extensive in the chapters on tropical diseases and the treatment of syphilis. There also have been added the newer findings in the rapidly growing field of dermatology.

Altogether the authors have succeeded in keeping their text up to the minute and have retained its position as one of the top reference books in dermatological literature.

JOHN C. GRAHAM

Scheuermann's Disease

Die Scheuermannsche Krankheit, und Ihre Differentialdiagnose. By J. E. W. Brocher. Basel, Switzerland, Benno Schwabe & Co., [c. 1946]. 8vo. 91 pages, illustrated. Paper, 11 fr.

This is a scholarly monograph on a comparatively young disease, Scheuermann's Kyphosis, covering every aspect of the affection. The fact that this harmless condition may be confused with serious affections makes it imperative for the physician to familiarize himself with the subject. The author fully attains his purpose. The chapter on differential diagnosis is of particularly practical interest and deserves special commendation.

S. W. WESTING

Geriatrics

The Years After Fifty. By Wingate M. Johnson, M.D. New York, Whittlesey House, [c. 1947]. 8vo. 153 pages. Cloth, $2.00.

This is another book in the Health Series by Whittlesey House, written for the layman. It is refreshing to see a book of this kind written by one who not only knows his stuff but knows how to present it without scaring the life out of people. Dr. Johnson deals with all the important problems of the aged in a typical Johnsonian style, full of humor, common sense, and good cheer. He makes it more than readable. Many laymen and physicians will use this book as a means of growing old more gracefully.

MALFORD W. THEWLIS

Psychiatry

Brief Psychotherapy. A Handbook for Physicians on the Clinical Aspects of Neuroses. By Bertrand S. Frohman, M.D. With the collaboration of Evelyn P. Frohman. Philadelphia, Lea & Febiger, [c. 1948]. 12mo. 265 pages. Cloth, $4.00.

A good handbook for the general practitioner who feels that he needs to refresh his knowledge of psychological medicine and its practical therapeutic applications. Written in concise textbook form with a good glossary, it makes very interesting reading.

C. MILTON MEEKS

Rh Factor

Der Rhesusfaktor. Seine Theoretische und Praktische Bedeutung. By Professor Dr. G. Fanconi, Professor Dr. A. Grumbach, Professor Dr. H. Willi, *et al.* Basel, Benno Schwabe & Co., [c 1946]. 8vo. 160 pages, illustrated. Paper, Sw. fr. 10.

This compact paper-covered book of 160 closely-printed pages covers the most important phases of the Rh Factor and its relationship to hemolytic disease of the newborn. Case histories are given in the minutest details: as is also the histopathology in the autopsy material. The book is well illustrated with photographs, line drawings and tables. Each chapter has a summary which is translated into French, Italian, and English. A bibliography follows each subject.

JACOB HALPERIN

Therapy

Treatment in General Practice. By Harry Beckman, M.D. 6th Edition. Philadelphia, W. B. Saunders Co., [c. 1948]. 8vo. 1,129 pages, illustrated. Cloth, $11.50.

In order to obtain some idea of the value of this work, the reviewer used it to look up the treatment of various conditions with which he is quite familiar. The treatment of cardiovascular syphilis, the use of anticoagulants and of propylthiouracil were all well presented. The management of congestive heart failure was very well done except that the use of quinidine sulfate should not have been presented in that section. Many other subjects were investigated with the result that in the opinion of the reviewer this book can be highly recommended as a useful and reliable addition to the physician's library.

EDWIN P. MAYNARD, JR.

Medical Times

The Journal of the American Medical Profession

INDEX

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CORRESPONDENCE

EDITORIALS

GENERAL PRACTICE

SPECIAL ARTICLES

SUBJECTS AND AUTHORS

ASSOCIATED PHYSICIANS OF LONG ISLAND

excursion into logic

Quae cum ita sint. (And since this is so.)

Premise No. 1: Progesterone products administered during pregnancy inhibit protection and utilization of endogenous progesterone, as indicated by diminished pregnanediol excretion, while estrogens have the opposite effect of stimulating production and utilization of progesterone. (Smith, Smith and Hurwitz[1], Meaker[2].)

Premise No. 2: Exogenous progesterone, even in combination with estrogens, frequently sensitize the myometrium to contractile action of posterior pituitary oxytocin, actually contributing toward abortion and premature delivery. (Bender[3], Vaux and Rakoff[4].)

Premise No. 3: High-dosage stilbestrol therapy gives higher percentage of protection of pregnancy in threatened and habitual abortion and in premature delivery than any method previously employed. (Karnaky[5], Rosenblum and Melinkoff[6].)

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References: 1. Smith, O. W.; Smith, G. van S., and Hurwitz, D.: Increased excretion of pregnanediol in pregnancy from diethylstilbestrol with special reference to the prevention of late pregnancy accidents, Am. J. Obst. & Gynec. *51*:411, 1946.

2. Meaker, S. R.: A working classification of the causes of abortion, J.A.M.A. *123*:680, 1943.

3. Bender, S.: The value of the Guterman test in threatened abortion, J. Obst. & Gynec. Brit. Emp. *54*:783, 1947.

4. Vaux, N. W., and Rakoff, A. E.: The treatment of habitual abortion with estrogen and progesterone, Surg. Clin. North America *25*:1324, 1945.

5. Karnaky, K. J.: Original gynecological and obstetrical research—sterility, endocrine and vaginal operations, M. Rec. & Ann. *35*:851, 1941.

6. Rosenblum, G., and Melinkoff, E.: Preservation of the threatened pregnancy with particular references to the use of diethylstilbestrol, West. J. Surg. Obst. & Gynec. *55*:597, 1947.

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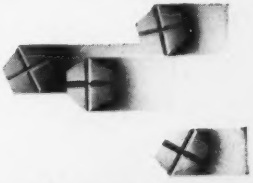

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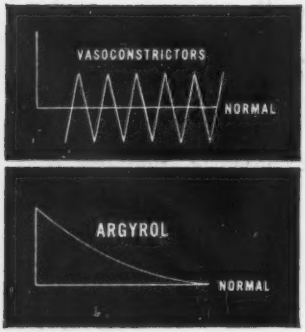

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